ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Vueway 0.5 mmol/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL of solution contains 485.1 mg gadopiclenol (equivalent to 0.5 mmol of gadopiclenol and to 78.6 mg of gadolinium).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, colourless to pale yellow solution

Mean osmolality at 37 °C	850 mOsm/kg H_2O
pH	7.0-7.8
Viscosity at 20 °C	12.5 mPa s
Viscosity at 37 °C	7.7 mPa s

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Vueway is indicated in adults and children aged 2 years and older for contrast-enhanced magnetic resonance imaging (MRI) to improve detection and visualization of pathologies with disruption of the blood-brain-barrier (BBB) and/or abnormal vascularity of:

- the brain, spine, and associated tissues of the central nervous system (CNS);
- the liver, kidney, pancreas, breast, lung, prostate, and musculoskeletal system.

It should be used only when diagnostic information is essential and not available with unenhanced MRI.

4.2 Posology and method of administration

This medicinal product should only be administered by trained healthcare professionals with technical expertise in performing gadolinium enhanced MRI.

Posology

The recommended dose of Vueway is 0.1 mL/kg body weight (BW) (equivalent to 0.05 mmol/kg BW) to provide diagnostically adequate contrast for all indications.

The dose should be calculated based on the patient's BW and should not exceed the recommended dose per kilogram of BW detailed in this section.

Table 1 below indicates the volume to be administered according to BW.

Table 1: Volume of Vueway to be administered per BW

BW kilograms (kg)	**Volume** millilitres (mL)	**Quantity** millimoles (mmol)
10	1	0.5
20	2	1.0
30	3	1.5
40	4	2.0
50	5	2.5
60	6	3.0
70	7	3.5
80	8	4.0
90	9	4.5
100	10	5.0
110	11	5.5
120	12	6.0
130	13	6.5
140	14	7.0

Elderly
No dose adjustment is necessary. Caution should be exercised in elderly patients (see section 4.4 and 5.2).

Renal impairment
No dose adjustment is necessary for patients with any level of renal impairment. Gadopiclenol should only be used in patients with severe renal impairment (GFR < 30 mL/min/1.73 m^2) and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI (see section 4.4). If it is necessary to use gadopiclenol, the dose should not exceed 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW). More than one dose should not be used during a scan. Because of the lack of information on repeated administration, gadopiclenol injections should not be repeated unless the interval between injections is at least 7 days.

Hepatic impairment
No dose adjustment is considered necessary for patients with hepatic impairment. Caution is recommended, especially in the case of perioperative liver transplantation period (see above "renal impairment").

Paediatric population (2 years and older)
The recommended and maximum dose of Vueway is 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) for all indications. More than one dose should not be used during a scan.

The safety and efficacy of Vueway in children less than 2 years has not yet been established. No data are available.

Method of administration

The medicinal product is for intravenous use only.

The recommended dose is administered intravenously as a bolus injection at approximatively 2 mL/sec followed by a flush of sodium chloride 9 mg/ml (0.9%), solution for injection via manual injection or power injector.

Intravenous administration of contrast agent should, if possible, be done with the patient lying down. Since experience shows that most undesirable effects occur within minutes after administration, the patient should be kept under observation during and following administration for at least half an hour (see section 4.4).

For instructions on the medicinal product before administration, see section 6.6.

Paediatric population
In children, Vueway in vials with a single use syringe of a volume adapted to the amount to be injected should be used in order to have better precision of the injected volume.

Image acquisition

Contrast-enhanced MRI can start after the injection depending on the pulse sequences used and the protocol for the examination. Optimal signal enhancement is generally observed during arterial phase and within a period of about 15 minutes after injection. Longitudinal relaxation times (T1)-weighted sequences are particularly suitable for contrast-enhanced examinations.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Gadopiclenol 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 of gadolinium-based contrast agents.

The usual precautions for MRI examination should be applied, such as exclusion of patients with pacemakers, ferromagnetic vascular clips, infusion pumps, nerve stimulators, cochlear implants, or suspected intracorporal metallic foreign bodies, particularly in the eye.

MRI images produced with this medicinal product should only be analysed and interpreted by the healthcare professionals trained in interpretation of gadolinium enhanced MRI.

There are no or limited clinical data investigating the performance of gadopiclenol for CNS imaging in patients with inflammatory, infectious, autoimmune or demyelinating disorders (such as multiple sclerosis), patients with acute or chronic infarct, or patients with intramedullary spine lesions.
There are also no or limited clinical data investigating the performance of gadopiclenol for body imaging in patients with inflammatory, infectious and autoimmune conditions, including acute/chronic pancreatitis, inflammatory bowel disease, inflammatory diseases of head and neck region and endometriosis.

Potential for hypersensitivity or anaphylactic reactions

- As with other gadolinium-containing contrast agents, hypersensitivity reactions can occur, including life-threatening. Hypersensitivity reactions may be either allergic (described as anaphylactic reactions when serious) or non-allergic. They can occur either immediately (less than 60 minutes) after injection or delayed (up to 7 days). Anaphylactic reactions occur immediately and can be fatal. They are independent of the dose, can occur after even the first dose of the product, and are often unpredictable.

- During the examination, supervision by a physician is necessary. If hypersensitivity reactions occur, administration of the contrast agent must be discontinued immediately and – if necessary – a specific therapy must be instituted. A venous access should thus be kept during the entire examination. To permit immediate emergency countermeasures, appropriate drugs (e.g. epinephrine and antihistamines), an endotracheal tube and a respirator should be ready at hand.
- The risk of hypersensitivity reaction may be higher in patients with a history of previous reaction to gadolinium-containing contrast agents, bronchial asthma or allergy.

Renal impairment and nephrogenic systemic fibrosis (NSF)

Prior to administration of gadopiclenol**,** it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests.

There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 mL/min/1.73 m^2). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with gadopiclenol, it should only be used in patients with severe renal impairment and in patients in the perioperative liver transplantation period after careful benefit/risk assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI.

Haemodialysis shortly after gadopiclenol administration may be useful at removing it from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis.

Elderly

As the renal clearance of gadopiclenol may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction. Caution should be exercised in patients with renal impairment (see section 4.2).

Seizures

As with other gadolinium-containing contrast agents, special caution is necessary in patients with a lowered threshold for seizures. All equipment and drugs necessary to counter convulsions occurring during the MRI examination must be made ready for use beforehand.

Extravasation

Caution during administration is necessary to avoid any extravasation. In case of extravasation, the injection must be stopped immediately. In case of local reactions, evaluation and treatment should be carried out as necessary.

Cardiovascular disease

In patients with severe cardiovascular disease gadopiclenol should only be administrated after careful risk benefit assessment because no data are available so far.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 15 mL, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant medicinal products to be taken into account

Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists decrease the efficacy of the mechanisms of cardiovascular compensation for blood pressure disorders. The physician must obtain information before injection of gadopiclenol about the concomitant intake of those medicinal products.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on the use of gadolinium-based contrast agents including gadopiclenol in pregnant women is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the foetus. Animal studies showed little placental transfer and do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Vueway should not be used during pregnancy unless the clinical condition of the woman requires use of gadopiclenol.

Breast-feeding

Gadolinium-containing contrast agents are excreted into breast milk in very small amounts. At clinical doses, no effects on the infant are anticipated due to the small amount excreted in milk and poor absorption from the gut. Continuing or discontinuing breast feeding for a period of 24 hours after administration of Vueway, should be at the discretion of the doctor and breast-feeding mother.

Fertility

Animals studies do not indicate impairment of fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Vueway has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequent adverse reactions were injection site pain, headache, nausea, injection site coldness, fatigue and diarrhoea.

Tabulated list of adverse reactions

Table 2 below presents adverse reactions based on clinical trials including 1047 subjects exposed to gadopiclenol ranging from 0.05 mL/kg BW (equivalent to 0.025 mmol/kg BW) to 0.6 mL/kg BW (equivalent to 0.3 mmol/kg BW).

The adverse reactions are listed below by SOC (System Organ Class) and by frequency with the following guidelines: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000).

Table 2: Adverse reactions reported following gadopiclenol administration

System Organ Class	Frequency	
	Common	**Uncommon**
Immune system disorders	-	Hypersensitivity*
Nervous system disorders	Headache	Dysgeusia
Gastrointestinal disorders	-	Diarrhoea, Nausea, Abdominal pain, Vomiting
General disorders and administration site conditions	Injection site reaction**	Fatigue, Feeling hot

* Including immediate (dermatitis allergic, erythema, dyspnoea, dysphonia, throat tightness, throat irritation, paraesthesia oral and flushing) and delayed (periorbital oedema, swelling, rash and pruritus) reactions.
** Injection site reaction includes the following terms: injection site pain, injection site oedema, injection site coldness, injection site warmth, injection site haematoma and injection site erythema.

Description of selected adverse reactions

Hypersensitivity
Immediate reactions include one or more effects, which appear simultaneously or sequentially, which are most often cutaneous, respiratory and/or vascular reactions. Each sign may be a warning sign of a starting shock and go very rarely to death.

Nephrogenic systemic fibrosis (NSF)
Isolated cases of NSF have been reported with other gadolinium-containing contrast agents (see section 4.4).

Paediatric population (2 years and older)

A total of 80 paediatric patients aged 2 years and older were included in the clinical trial.
As compared to adults, the safety profile of gadopiclenol in this population did not show any specific safety concern.

A total of 31 Treatment Emergent Adverse Events (TEAEs) occurred during and/or after gadopiclenol administration for 14 patients (17.5%). Twelve TEAEs were reported in the CNS cohort and 2 in the Body cohort.
Among these TEAEs, 1 event in 1 patient (1.25%) from the CNS cohort was considered related to gadopiclenol.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

The maximum daily single dose tested in humans was 0.6 mL/kg BW (equivalent to 0.3 mmol/kg BW), which corresponds to 6 times the recommended dose.

No signs of intoxication from an overdose have so far been reported.

Gadopiclenol can be removed by haemodialysis. However, there is no evidence that haemodialysis is suitable for prevention of nephrogenic systemic fibrosis (NSF).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: paramagnetic contrast media, ATC code: V08CA12.

Gadopiclenol is a paramagnetic agent for Magnetic Resonance Imaging (MRI).

Mechanism of action

The contrast-enhancing effect is mediated by gadopiclenol which is a macrocyclic non-ionic complex of gadolinium, the active moiety which enhances the relaxation rates of water protons in its vicinity in the body, leading to an increase in signal intensity (brightness) of tissues.

When placed in a magnetic field (patient in MRI machine), gadopiclenol shortens the T_1 and T_2 relaxation times in targeted tissues. The extent to which a contrast agent can affect the relaxation rate of tissue water ($1/T_1$ or $1/T_2$) is termed relaxivity (r_1 or r_2).

Gadopiclenol presents a high relaxivity in water (see Table 3) due to its chemical structure, because it can exchange two water molecules, which are linked to the gadolinium to complete its coordination number in addition to the four nitrogens and the three oxygens of the carboxylate functions of the gadopiclenol chelate. This explains that, gadopiclenol given at half dose of gadolinium compared to other non-specific gadolinium-containing contrast agents, may provide the same contrast enhancement.

Table 3: Relaxivity at 37 °C for gadopiclenol

	r_1 ($mmol^{-1}.l.s^{-1}$)			**r_2 ($mmol^{-1}.l.s^{-1}$)**		
Magnetic field	**0.47 T**	**1.5 T**	**3 T**	**0.47 T**	**1.5 T**	**3 T**
Relaxivity in water	12.5	12.2	11.3	14.6	15.0	13.5
Relaxivity in biological medium	13.2	12.8	11.6	15.1	15.1	14.7

Clinical efficacy and safety

Two pivotal studies included adult patients undergoing MRI with gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) and MRI with gadobutrol at 0.1 mL/kg BW (equivalent to 0.1 mmol/kg BW). One study (Study 1; PICTURE) included 256 patients presenting with known or highly suspected CNS lesions with focal areas of disrupted BBB (e.g. primary and secondary tumors). The majority of patients (72%) presented with brain tumors, 20% had brain or spine metastases and 8% presented with other pathologies.

The other study (Study 2; PROMISE) included 304 patients with known or suspected abnormalities or lesions in other body regions (8% in head and neck, 28% in thorax, 35% in abdomen, 22% in pelvis and 7% in musculo-skeletal system) both based on results of a previous imaging procedure such as CT or MRI. The most frequent pathologies were breast tumors (23%) and liver tumors (21%).

The primary endpoint was the evaluation of lesion visualization, based on 3 co-criteria (border delineation, internal morphology and degree of contrast enhancement) by three independent blinded readers, using a 4-point scale. The mean of scores for each of the 3 lesion visualization co-criteria was calculated as the sum of scores for up to 3 most representative lesions divided by the number of lesions.

Both studies demonstrated:

- Superiority of the combined unenhanced/contrast-enhanced MRI (Paired) with gadopiclenol over unenhanced MRI (Pre) for all 3 lesion visualization criteria ($p < 0.0001$ for all three readers, paired t-tests on matching lesions).
- Non-inferiority of gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) to gadobutrol at 0.1 mL/kg BW (equivalent to 0.1 mmol/kg BW) ($p < 0.0001$ for all three readers, paired t-tests on matching lesions).

The pooled analysis of the primary outcome over the three readers, and for each lesion visualization criterion also demonstrated the non-inferiority of gadopiclenol at 0.05 mmol/kg to gadobutrol at 0.1 mmol/kg in both studies, as shown in table 4 below.

Table 4: Lesion visualization – Off-site readings – Full analysis set

	n patients	LS Mean (SE)			95% CI difference	p-value
		Gadopiclenol	Gadobutrol	Difference		
Study 1 (PICTURE)						
Border delineation	239	3.83 (0.02)	3.82 (0.02)	0.01 (0.02)	[-0.02 ; 0.05]	0.5025
Internal morphology	239	3.83 (0.02)	3.81 (0.02)	0.02 (0.02)	[-0.01 ; 0.05]	0.2006
Degree of contrast enhancement	239	3.73 (0.03)	3.68 (0.03)	0.05 (0.02)	[0.01 ; 0.09]	0.0172
Study 2 (PROMISE)						
Border delineation	273	3.60 (0.03)	3.60 (0.03)	-0.00 (0.02)	[-0.05 ; 0.04]	0.8987
Internal morphology	273	3.75 (0.02)	3.76 (0.02)	-0.01 (0.02)	[-0.05 ; 0.03]	0.6822
Degree of contrast enhancement	273	3.30 (0.04)	3.29 (0.04)	0.01 (0.03)	[-0.05 ; 0.07]	0.8546

CI: Confidence Interval ; LS: Least Squares ; SE: Standard Error.

The secondary criteria evaluated included quantitative evaluations (Contrast to Noise Ratio, Lesion to Brain (background) Ratio and percentage of lesion enhancement), overall diagnostic preference and impact on patient management.

In Study 1, Lesion to Brain Ratio, and percentage of lesion enhancement were statistically significantly higher with gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) compared to gadobutrol at 0.1 mL/kg BW (equivalent to 0.1 mmol/kg BW) for all 3 readers. Contrast to Noise Ratio was statistically significantly higher for 2 readers. In Study 2, percentage of lesion enhancement was significantly higher with gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) compared to gadobutrol at 0.1 mL/kg BW (equivalent to 0.1 mmol/kg BW) and no statistically significant difference was observed for Lesion to Background Ratio.

Lesion visualisation parameters (e.g., co-primary endpoints and quantitative assessments, such as, Contrast to Noise Ratio, Lesion to Brain (background) Ratio and percentage of lesion enhancement) were assessed in all the lesions identified by the blinded readers, independently of their size, in more than 86% of patients in CNS study and in more than 81% of patients in Body study, who had no more than 3 lesions. In the remaining patients with more than 3 lesions visible, a subset of 3 most representative lesions were selected for assessment of the co-primary endpoints. Therefore, in those patients, the additional lesions were not assessed. Consequently, the technical capability of lesion visualisation for both contrast agents cannot be extrapolated for those non-selected lesions.

The overall diagnostic preference was assessed in a global matched-pairs fashion (reading of images from both MRI assessed side by side) by three additional blinded readers in each study. The results are summarized in the Table 5 below. In Study 1, in majority, the readers expressed a preference for images acquired with gadopiclenol. In Study 2, in majority, the readers expressed no diagnostic preference between images acquired with gadopiclenol and with gadobutrol.

Table 5: Results on overall diagnostic preference for Study 1 (CNS) and Study 2 (Body)

	Reader	N	gadopiclenol preferred	No preference	gadobutrol preferred	p-value*
Study 1 (CNS)	4	241	108 (44.8 %)	98 (40.7 %)	35 (14.5 %)	< 0.0001
	5	241	131 (54.4 %)	52 (21.6 %)	58 (24.1 %)	< 0.0001
	6	241	138 (57.3 %)	56 (23.2 %)	47 (19.5 %)	< 0.0001
Study 2 (Body)	4	276	36 (13.0 %)	216 (78.3 %)	24 (8.7 %)	0.1223
	5	276	40 (14.5 %)	206 (74.6 %)	30 (10.9 %)	0.2346
	6	276	33 (12.0 %)	228 (82.6 %)	15 (5.4 %)	0.0079

* Wilcoxon signed-rank test.

A change in patient treatment plan was reported after administration of gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) in 23.3 % and 30.1 % of patients in Study 1 and Study 2, respectively. Analysis per subgroups in Study 1 revealed that treatment plan could be changed for 64 % of the 22 patients for whom the investigator considered that diagnosis was not assessable (or grade of glial tumor could not be determined) based on unenhanced MRI, 28 % of 81 patients with malignant diagnosis and about 12 % of 111 patients with non-malignant diagnosis.

In Study 2, treatment plan could be changed after MRI with gadopiclenol for 41 % of the 22 patients with non-assessable diagnosis based on unenhanced MRI, 32 % of 165 patients with malignant diagnosis and 14 % of 64 patients with non-malignant diagnosis.

A post-hoc reading of all images from both pivotal studies for CNS and Body indications was conducted in a fully blinded, unpaired, randomised manner . A high level of concordance in lesion detectability between gadopiclenol at 0.05 mmol/kg and gadobutrol at 0.1 mmol/kg was observed at lesion and at patient level. The results are summarized in Table 6 below.

Table 6: Concordance in lesion detectability between gadopiclenol at 0.05 mmol/kg and gadobutrol at 0.1 mmol/kg

	Perfect match at lesion level*	**Perfect match at patient level***
Study 1 (CNS)	88.0% to 89.8%	84.3% to 86.0%
Study 2 (Body) overall	92.3% to 95.5%	81.3% to 85.0%
Head & Neck	89.5% to 100%	70.6% to 94.1%
Thorax	88.3% to 93.2%	69.8% to 73.2%
Pelvis	91.7% to 100%	87.5% to 94.6%
Abdomen	94.6% to 95.2%	84.0% to 87.2%
Musculoskeletal	100%	100%

*Range of values according to the reader (3 readers per region)

Paediatric population
One exploratory study (Study 3) with a single dose of gadopiclenol (0.1 mL/kg BW equivalent to 0.05 mmol/kg BW) included 80 paediatric patients aged 2 to 17 years old with 60 patients undergoing CNS MRI and 20 patients undergoing Body MRI.
Diagnostic efficacy was evaluated and there was no difference among the paediatric age groups.

The European Medicines Agency has deferred the obligation to submit the results of studies with Vueway in one or more subsets of the paediatric population in the detection and visualisation of disorders or lesions with suspected abnormal vascularity in various body regions for diagnostic purposes. (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The absolute bioavailability of gadopiclenol (in humans) is 100%, as it is only administered via the intravenous route.

After an intravenous dose of 0.1 to 0.2 mL/kg BW (equivalent respectively to 0.05 and 0.1 mmol/kg BW), the C_{max} was 525 ± 70 mcg/mL and 992 ± 233 mcg/mL, respectively.

The C_{max} increased 1.1-fold, 1.1-fold and 1.4-fold and the AUC_{inf} increased 1.5-fold, 2.5-fold and 8.7-fold in patients with mild, moderate and severe renal impairment, respectively after a dose of 0.2 mL/kg BW (equivalent to 0.1 mmol/kg BW).

In addition, the increase in C_{max} and AUC_{inf} is expected to be similar with a dose of 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) based on the results of population pharmacokinetic simulations.

Distribution

After intravenous administration gadopiclenol is rapidly distributed in the extracellular fluids.
After a dose of 0.1 ml/kg BW (equivalent to 0.05 mmol/kg BW) the distribution volume Vd was 12.9 ± 1.7 L.
The *in vitro* binding of 153Gd-gadopiclenol to human plasma proteins is negligible and independent of the gadopiclenol concentration, as 153Gd-gadopiclenol bound 0.0–1.8% to human plasma proteins and 0.0-0.1% to human red blood cells.

Biotransformation

Gadopiclenol is not metabolised.
The lack of metabolism is confirmed by *in vitro* data using pooled human liver microsomes incubated with 153Gd-gadopiclenol. After 120 minutes ≥ 95% of the 153Gd-gadopiclenol remained in unchanged form. The results were similar when heat inactivated pooled human liver microsomes (negative controls) were incubated with 153Gd-gadopiclenol, indicating that 153Gd-gadopiclenol is not metabolised.

Elimination

Gadopiclenol is eliminated rapidly in unchanged form through the kidneys by glomerular filtration. After a dose of 0.1 to 0.2 mL/kg BW (equivalent respectively to 0.05 and 0.1 mmol/kg BW), the mean plasma elimination half-life ($t_{1/2}$) in healthy volunteers with a normal renal function was1.5 and 1.7 hour, respectively, and the clearance was 100 ± 10 mL/min and 96 ± 12 mL/min, respectively. Urinary excretion is the major route of elimination of gadopiclenol, with approximately 98 % of the dose excreted in urine after 48 hours regardless of the dose administered.

Linearity/non-linearity

The pharmacokinetic profile of gadopiclenol is linear in the studied dose range (0.05 to 0.6 mL/kg BW equivalent to 0.025 to 0.3 mmol/kg BW), without difference between males and females. Mean maximum concentration (C_{max}) and Area Under the Curve (AUC_{inf}) increased proportionally to the dose.

Paediatric population

One Phase II study (Study 3) with a single dose of gadopiclenol at 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) was conducted and included 60 paediatric patients aged 2 to 17 years old undergoing CNS MRI.

Individual parameters predicted from the population pharmacokinetic model and normalised by BW were similar between adults and children. The terminal half-life was 1.77 hour for age group 12-17 years old, 1.48 hour for age group 7-11 years old and 1.29 hour for age group 2-6 years old. The median clearance ranged from 0.08 L/h/kg (for age group 12-17 years old) to 0.12 l/h/kg (for age group 2-11 years old).

The pharmacokinetics of gadopiclenol in children aged 2 to 17 years are comparable to the pharmacokinetics in adults.

Renal impairment and dialysability

The elimination half-life ($t_{1/2}$) is prolonged in subjects with renal impairment, increasing with the degree of renal impairment. In patients with mild ($60 \leq$ eGFR < 90 mL/min), moderate ($30 \leq$ eGFR < 60 mL/min) and severe ($15 \leq$ eGFR < 30 mL/min) renal impairment, the mean $t_{1/2}$ was 3.3, 3.8 and 11.7 hours, respectively and the clearance was 1.02, 0.62 and 0.17 mL/min/kg, respectively.

The C_{max} increased 1.1-fold, 1.1-fold and 1.4-fold and the AUC_{inf} increased 1.5-fold, 2.5-fold and 8.7-fold in patients with mild, moderate and severe renal impairment, respectively after a dose of 0.2 mL/kg BW (equivalent to 0.1 mmol/kg BW).

In addition, the increase in C_{max} and AUC_{inf} is expected to be similar with a dose of 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW) based on the results of population pharmacokinetic simulations.

Urinary excretion is delayed with the progression of renal impairment level. In patients with mild or moderate renal impairment, more than 90 % of the administered dose was recovered in the urine within 48 hours. In patients with severely impaired renal function about 84 % of the administered dose was recovered in the urine within 5 days.

In patients with End Stage Renal Disease (ESRD), 4 hour haemodialysis effectively removed gadopiclenol from plasma as the percentage of decrease in blood concentrations was 95 to 98 % at the end of the first haemodialysis session.

Weight

The effect of weight was investigated with population pharmacokinetic simulations of patients with a BW ranging from 40 kg to 150 kg receiving a gadopiclenol dose of 0.1 mL/kg BW (equivalent to 0.05 mmol/kg BW). The ratios of median AUC_{inf} of gadopiclenol between a typical healthy subject of 70 kg and subjects weighing 40 kg and 150 kg was 0.86 and 2.06, respectively. The ratios of the plasma concentrations 10, 20 and 30 minutes after administration between a typical healthy subject of 70 kg and subjects weighing 40 kg and 150 kg ranged from 0.93 to 1.26.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

Juvenile animal toxicity studies have not revealed any relevant findings.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tetraxetan
Trometamol
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

For vials

Chemical and physical in-use stability has been demonstrated for 24 hours at up to 25 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless the opening has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

For vials

This medicinal product does not require any special storage conditions.

For storage conditions after first opening of the medicinal product, see section 6.3.

For pre-filled syringes

Do not freeze.

6.5 Nature and contents of container

3 mL solution for injection in a 10 mL vial (glass type I) with elastomeric stopper in pack size of 1.

7.5 mL solution for injection in a 10 mL vial (glass type I) with elastomeric stopper in pack sizes of 1 or 25.

10 mL solution for injection in a 10 mL vial (glass type I) with elastomeric stopper in pack sizes of 1 or 25.

15 mL solution for injection in a 20 mL vial (glass type I) with elastomeric stopper in pack sizes of 1 or 25.

30 mL solution for injection in a 50 mL vial (glass type I) with elastomeric stopper in pack size of 1.

50 mL solution for injection in a 50 mL vial (glass type I) with elastomeric stopper in pack size of 1.

100 mL solution for injection in a 100 mL vial (glass type I) with elastomeric stopper in pack size of 1.

7.5 mL, 10 mL or 15 mL of solution for injection in a 15 mL plastic (polypropylene) pre-filled syringe, graduated every 0.5 mL, without a needle, with an elastomeric (bromobutyl) plunger stopper and capped with an elastomeric (bromobutyl) tip cap. Pack size of 1 or a multipack containing 10 (10 packs of 1) pre-filled syringes.

7.5 mL, 10 mL or 15 mL of solution for injection in 15 a mL plastic (polypropylene) pre-filled syringe, graduated every 0.5 mL, with an elastomeric (bromobutyl) plunger stopper and capped with an elastomeric (bromobutyl) tip cap with administration set for manual injection (one extension line and one catheter) in pack size of 1.

7.5 mL, 10 mL or 15 mL of solution for injection in 15 mL plastic (polypropylene) pre-filled syringe, graduated every 0.5 mL, with an elastomeric (bromobutyl) plunger stopper and capped with an elastomeric (bromobutyl) tip cap with administration set for Optistar Elite injector (one extension line, one catheter and one empty 60 mL plastic syringe) in pack size of 1.

7.5 mL, 10 mL or 15 mL of solution for injection in 15 mL plastic (polypropylene) pre-filled syringe, graduated every 0.5 mL, with an elastomeric (bromobutyl) plunger stopper and capped with an elastomeric (bromobutyl) tip cap with administration set for Medrad Spectris Solaris EP injector (one extension line, one catheter and one empty 115 mL plastic syringe) in pack size of 1.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Do not use if the medicinal product including packaging is opened or damaged.

The solution for injection should be inspected visually prior to use.

Solution with visible signs of deterioration (such as particles in the solution, fissures in the vial) must not be used.

Before and during the use of the product, follow the safety, hygiene and asepsis rules.

For vials

The vial stopper should be pierced only once.

For pre-filled syringes

Do not use the pre-filled syringe if there are any signs of leakage.

The pre-filled syringe is for single use only. Do not attempt to re-use even after cleaning or sterilizing the single use pre-filled syringe.

Screw the push rod into the syringe plunger. It is important to rotate and push the push rod an additional ½ turn so that the plunger can rotate freely.
Before using the pre-filled syringe, remove the tip cap by spinning it.
Connection is compatible with luer 6%.
All luer connections should be gently hand tightened without over tightening to ensure secure connection and to prevent damage to the device.
Before connecting to the patient, prime completely the intravenous line and check the absence of air: hold the syringe erect and push plunger forward until all of the air is evacuated and fluid either appears at the tip of the needle or the tubing is filled.

The dose volume accuracy has been checked and is conform to ISO 7886-1.
The delivered dose accuracy for 15 mL syringes, graduated every 0.5 mL, depends on the injected volume. For a volume range of 5 to 15 mL, it may vary up to ± 0.6 mL.

When used with a power injector, follow injector instructions for use.

Any unused product should be discarded at the end of the examination session.

The peel-off tracking label available on the vial or the pre-filled syringe should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record.

Any unused portions and waste material derived from disposal and items which come into contact with the product when administering this product with an automatic application system should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bracco Imaging SPA
Via Egidio Folli, 50
20134 Milan
Italy

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1773/001-025

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 December 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Guerbet
16 rue Jean Chaptal
93600 Aulnay-sous-Bois
France

BIPSO GmbH
Robert-Gerwig-Strasse 4
Singen (Hohentwiel)
78224
Germany

Bracco Imaging S.p.A.
Bioindustry Park, Via Ribes 5
10010 Colleretto Giacosa (TO)
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

Text for the carton box (outer packaging) of 3 mL, 7.5 mL, 10 mL, 15 mL, 30 mL, 50 mL and 100 mL vial for all pack sizes.
The outer label contains Blue box.

Text for the inner label (immediate packaging) of 15 mL, 30 mL, 50 mL and 100 mL vial.
No Blue box is included in the inner label.

1. NAME OF THE MEDICINAL PRODUCT

Vueway 0.5 mmol/mL solution for injection
gadopiclenol

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mL of solution contains 485.1 mg gadopiclenol (equivalent to 0.5 mmol of gadopiclenol and to 78.6 mg of gadolinium).

3. LIST OF EXCIPIENTS

Excipients: tetraxetan, trometamol, hydrochloric acid, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

On the outer carton:
Single pack:
1 vial of 3 mL
1 vial of 7.5 mL
1 vial of 10 mL
1 vial of 15 mL
1 vial of 30 mL
1 vial of 50 mL
1 vial of 100 mL

Other pack:
25 vials of 7.5 mL
25 vials of 10 mL
25 vials of 15 mL

On the inner label:
15 mL
30 mL
50 mL
100 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Not applicable.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Not applicable.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bracco Imaging SPA
Via Egidio Folli, 50
20134 Milan
Italy
(logo)

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1773/001 1 vial of 3 mL
EU/1/23/1773/002 1 vial of 7.5 mL
EU/1/23/1773/003 25 vials of 7.5 mL
EU/1/23/1773/004 1 vial of 10 mL
EU/1/23/1773/005 25 vials of 10 mL
EU/1/23/1773/006 1 vial of 15 mL
EU/1/23/1773/007 25 vials of 15 mL
EU/1/23/1773/008 1 vial of 30 mL
EU/1/23/1773/009 1 vial of 50 mL

EU/1/23/1773/010 1 vial of 100 mL

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Not applicable.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Text for the inner label (immediate packaging) of 3 mL, 7.5 mL and 10 mL vial.

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vueway 0.5 mmol/mL Injection
gadopiclenol
IV use

2. METHOD OF ADMINISTRATION

Not applicable.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL
7.5 mL
10 mL

6. OTHER

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

Text for the carton box (outer packaging) of 7.5 mL, 10 mL and 15 mL pre-filled syringe for single pack and multipack.
The outer label contains Blue box.

Text for the inner label (immediate packaging) of 15 mL pre-filled syringe.
No Blue box is included in the inner label.

1. NAME OF THE MEDICINAL PRODUCT

Vueway 0.5 mmol/mL solution for injection
gadopiclenol

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mL of solution contains 485.1 mg gadopiclenol (equivalent to 0.5 mmol of gadopiclenol and to 78.6 mg of gadolinium).

3. LIST OF EXCIPIENTS

Excipients: tetraxetan, trometamol, hydrochloric acid, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

On the outer carton:
Single pack:
1 pre-filled syringe of 7.5 mL
1 pre-filled syringe of 10 mL
1 pre-filled syringe of 15 mL
1 pre-filled syringe of 7.5 mL with administration set for manual injection (extension line + catheter)
1 pre-filled syringe of 10 mL with administration set for manual injection (extension line + catheter)
1 pre-filled syringe of 15 mL with administration set for manual injection (extension line + catheter)

1 pre-filled syringe of 7.5 mL with administration set for Optistar Elite injector (extension line + catheter + empty 60-mL syringe)
1 pre-filled syringe of 10 mL with administration set for Optistar Elite injector (extension line + catheter + empty 60-mL syringe)
1 pre-filled syringe of 15 mL with administration set for Optistar Elite injector (extension line + catheter + empty 60-mL syringe)

1 pre-filled syringe of 7.5 mL with administration set for Medrad Spectris Solaris EP injector (extension line + catheter + empty 115-mL syringe)
1 pre-filled syringe of 10 mL with administration set for Medrad Spectris Solaris EP injector (extension line + catheter + empty 115-mL syringe)
1 pre-filled syringe of 15 mL with administration set for Medrad Spectris Solaris EP injector (extension line + catheter + empty 115-mL syringe)

Multipack:
10 pre-filled syringes of 7.5 mL
10 pre-filled syringes of 10 mL
10 pre-filled syringes of 15 mL

On the inner label:
15 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Not applicable.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bracco Imaging SPA
Via Egidio Folli, 50
20134 Milan
Italy
(logo)

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1773/011 1 pre-filled syringe of 7.5 mL
EU/1/23/1773/012 10 (10 x 1) pre-filled syringes of 7.5 mL (multipack)

EU/1/23/1773/013 1 pre-filled syringe of 7.5 mL + administration set for manual injection (1 extension line + 1 catheter)
EU/1/23/1773/014 1 pre-filled syringe of 7.5 mL + administration set for Optistar Elite injector (1 extension line + 1 catheter +1 syringe of 60 ml)
EU/1/23/1773/015 1 pre-filled syringe of 7.5 mL + administration set for Medrad Spectris Solaris EP injector (1 extension line + 1 catheter +1 syringe of 115 ml)
EU/1/23/1773/016 1 pre-filled syringe of 10 mL
EU/1/23/1773/017 10 (10 x 1) pre-filled syringes of 10 mL (multipack)
EU/1/23/1773/018 1 pre-filled syringe of 10 mL + administration set for manual injection (1 extension line + 1 catheter)
EU/1/23/1773/019 1 pre-filled syringe of 10 mL + administration set for Optistar Elite injector (1 extension line + 1 catheter +1 syringe of 60 ml)
EU/1/23/1773/020 1 pre-filled syringe of 10 mL + administration set for Medrad Spectris Solaris EP injector (1 extension line + 1 catheter + 1 syringe of 115 ml)
EU/1/23/1773/021 1 pre-filled syringe of 15 mL
EU/1/23/1773/022 10 (10 x 1) pre-filled syringes of 15 mL (multipack)
EU/1/23/1773/023 1 pre-filled syringe of 15 mL + administration set for manual injection (1 extension line + 1 catheter)
EU/1/23/1773/024 1 pre-filled syringe of 15 mL + administration set for Optistar Elite injector (1 extension line + 1 catheter +1 syringe of 60 ml)
EU/1/23/1773/025 1 pre-filled syringe of 15 mL + administration set for Medrad Spectris Solaris EP injector (1 extension line + 1 catheter +1 syringe of 115 ml)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Not applicable.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
Text for the inner label (immediate packaging) of 7.5 mL and 10 mL pre-filled syringe.

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vueway 0.5 mmol/mL Injection
gadopiclenol
IV use

2. METHOD OF ADMINISTRATION

Not applicable.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

7.5 mL
10 mL

6. OTHER

Not applicable.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Vueway 0.5 mmol/mL solution for injection
gadopiclenol

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, radiologist or pharmacist.
- If you get any side effects, talk to your doctor, radiologist or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Vueway is and what it is used for

Vueway is a contrast agent which enhances the contrast of the images obtained during magnetic resonance imaging (MRI) examinations. Vueway contains the active substance gadopiclenol.

It improves the visualisation and delineation of abnormal structures or lesions of certain parts of the body and helps in the differentiation between healthy and diseased tissue.
It is used in adults and children (2 years of age and older).

It is given as an injection into your vein. This medicine is for diagnostic use only and will only be administered by healthcare professionals experienced in the field of clinical MRI practice.

2. What you need to know before you are given Vueway

Vueway must not be given to you
- if you are allergic to gadopiclenol or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, radiologist or pharmacist before you are given Vueway:
- if you had a previous reaction to any contrast agent,
- if you have asthma,
- if you have a history of allergy (such as hay fever, hives),
- if your kidneys do not work properly,
- ifyou had seizures (fits) or are being treated for epilepsy,
- if you have a disease affecting your heart or your blood vessels.

In all these cases, your doctor will decide whether the intended examination is possible or not. If you are given Vueway, your doctor or radiologist will take the necessary precautions and the administration of it will be carefully monitored.

Your doctor or radiologist may decide to take a blood test to check how well your kidneys are working before making the decision to use Vueway, especially if you are 65 years of age or older.

Other medicines and Vueway
Tell your doctor, radiologist or pharmacist if you are taking, have recently taken or might take any other medicines.
In particular, please inform your doctor, radiologist or pharmacist if you are taking or have recently taken medicines for heart and blood pressure disorders such as beta-blocking agents, vasoactive substances, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists.

Pregnancy and breast-feeding

Pregnancy
Gadopiclenol can cross the placenta. It is not known whether it affects the baby. Tell your doctor or radiologist if you think you are, or might become pregnant as Vueway should not be used during pregnancy unless strictly necessary.

Breast-feeding
Tell your doctor or radiologist if you are breast-feeding or about to start breast-feeding.
Your doctor will discuss whether you should continue or interrupt breast-feeding for a period of 24 hours after you receive Vueway.

Driving and using machines
Vueway has no or negligible effect on the ability to drive and use machines. However, if you feel unwell after the examination, you should not drive or use machines.

Vueway contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 15 mL vial, that is to say essentially 'sodium-free'.

3. How Vueway will be given to you

Vueway will be injected into your vein using a small needle by a specialised healthcare professional.
It can be administered by hand or by an automatic injector.

Your doctor or radiologist will determine the dose you will receive and supervise the injection.
The usual dose of 0.1 mL/kg body weight is the same in adults and children of 2 years and older.

In children, your doctor or radiologist will use Vueway in vials with a single use syringe to be able to have a better precision of the injected volume.

After the injection, you will be kept under supervision for at least 30 minutes. This is the time where most undesired reactions (such as allergic reactions) may occur. However, in rare cases, reactions may occur after hours or days.

Use in patients with severe kidney problems
The use of Vueway is not recommended in patients with severe kidney problems. However, if it is required you should only receive one dose of Vueway during a scan and you should not receive a second injection for at least 7 days.

Use in elderly
It is not necessary to adjust your dose if you are 65 years of age or older, but you may have a blood test to check how well your kidneys are working.

If you receive more Vueway than you should
It is highly unlikely that you will receive an overdose of Vueway, as it will be given to you by a trained healthcare professional. If it does happen, Vueway can be removed from the body by haemodialysis (blood cleaning).

If you have any further questions on the use of this medicine, ask your doctor, radiologist or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

After the administration of Vueway, you will be kept under observation. Most side effects occur within minutes. There is a small risk that you may have an allergic reaction to it. These effects can occur immediately and up to seven days after the injection. Such reactions can be severe and result in shock (case of allergic reaction that could put your life in danger).

Tell your doctor, radiologist or health professional immediately if you get any of the following side effects as it may be the first signs of a shock:
- swelling of the face, lips, tongue or throat
- lightheadedness (low blood pressure)
- breathing difficulties
- skin rash
- coughing, sneezing or runny nose

Possible side effects which have been observed during clinical trials with Vueway are listed below by how likely they are:

Frequency	**Possible side effects**
Common (may affect up to 1 in 10 people)	Injection site reaction* Headache
Uncommon (may affect up to 1 in 100 people)	Allergic reaction** Diarrhoea Nausea (feeling sick) Fatigue (tiredness) Abdominal pain Unusual taste in the mouth Feeling of warmth Vomiting (being sick)

*Injection site reaction includes: pain, swelling, cold feeling, warm feeling, bruising or redness.
**Allergic reaction may include: inflammation of the skin, reddening of the skin, breathing difficulties, voice impairment, throat tightness, throat irritation, abnormal sensation in the mouth, transient reddening of the face (early reactions) and puffy eyes, swelling, rash and itching (late reactions).

There have been reports of nephrogenic systemic fibrosis (NSF) (which causes hardening of the skin and may affect also soft tissue and internal organs) with other contrast agent containing gadolinium however no NSF case has been reported with Vueway during the clinical trials.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Vueway

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial or pre-filled syringe label and the carton box after "EXP". The expiry date refers to the last day of that month.

This medicine is a clear, colorless to pale yellow solution.
Do not use this medicine if the solution is not clear or if it contains visible particles.

For vials: This medicine does not require any special storage conditions.
Chemical and physical in-use stability has been demonstrated for 24 hours at up to 25 °C. From a microbiological point of view, the product should be used immediately after opening.

For pre-filled syringes: Do not freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Vueway contains
- The active substance is gadopiclenol. Each mL of solution contains 485.1 mg gadopiclenol (equivalent to 0.5 mmol of gadopiclenol and to 78.6 mg of gadolinium).
- The other ingredients are tetraxetan, trometamol, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and water for injections. See section 2 "Vueway contains sodium"

What Vueway looks like and contents of the pack

It is a clear, colourless to pale yellow solution for injection.

It is available in packs including:
- 1 vial containing 3, 7.5, 10, 15, 30, 50 or 100 mL of solution for injection.
- 25 vials containing 7.5, 10 or 15 mL of solution for injection.
- 1 or 10 (10 x 1) pre-filled syringes containing 7.5, 10 or 15 mL of solution for injection.
- 1 pre-filled syringe containing 7.5, 10 or 15 mL of solution for injection with administration set for manual injection (one extension line and one catheter).
- 1 pre-filled syringe containing 7.5, 10 or 15 mL of solution for injection with administration set for Optistar Elite injector (one extension line, one catheter and one empty 60 mL-plastic syringe).
- 1 pre-filled syringe containing 7.5, 10 or 15 mL of solution for injection with administration set for Medrad Spectris Solaris EP injector (one extension line, one catheter and one empty 115 mL-plastic syringe).

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Bracco Imaging SPA
Via Egidio Folli, 50
20134 Milan
Italy

Manufacturer
Guerbet
16 rue Jean Chaptal
93600 Aulnay-sous-Bois
France

BIPSO GmbH,
Robert-Gerwig-Strasse 4
Singen (Hohentwiel)
78224,
Germany

Bracco Imaging S.p.A.
Bioindustry Park, Via Ribes 5
10010 Colleretto Giacosa (TO)
Italy

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

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The following information is intended for healthcare professionals only:

For details on how to use the product, please refer to the section 6.6 Special precautions for disposal and other handling of the Summary of Product Characteristics of this product.