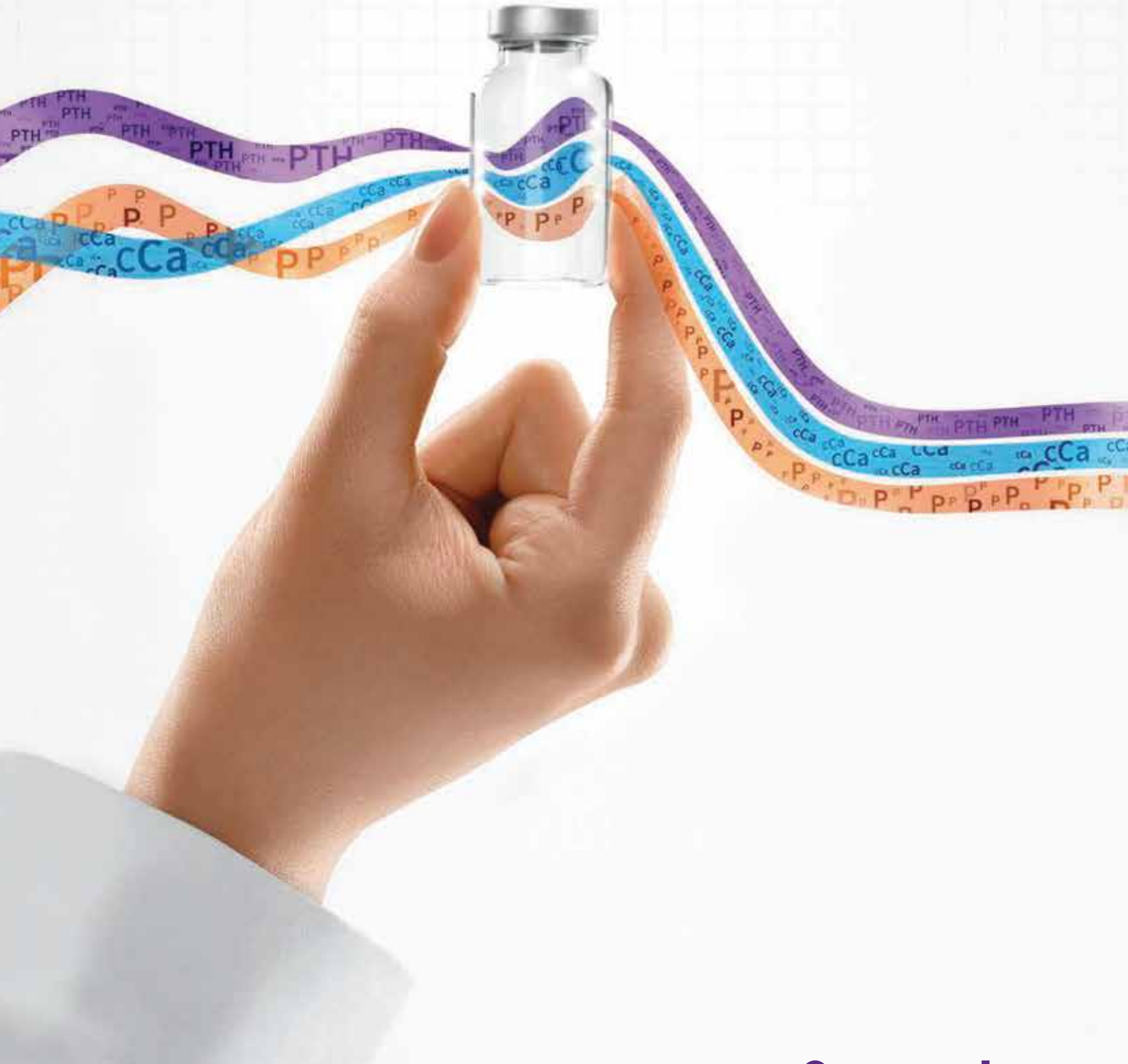
Parsabiv® (etelcalcetide) initiation considerations for your practice



Not an actual Parsabiv® vial. The displayed vial is for illustrative purposes only.

Parsabiv®
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Getting started with Parsabiv®

How to switch from cinacalcet to Parsabiv®

Ensure your patient discontinues use of cinacalcet tablets for at least 7 days prior to starting Parsabiv®[1]

Pills are not actual size

7-day discontinuation of cinacalcet

Initiate Parsabiv® after day 7, if corrected serum calcium is at or above lower limit of normal*

Initiating patients on Parsabiv®[1]

5 mg starting dose | **3x** a week | **During rinse back or IV after rinse back**

- Ensure corrected serum calcium is at or above the lower limit of normal prior to Parsabiv® initiation, a dose increase, or reinitiation after dosing interruption
- Initiate Parsabiv® at 5 mg, 3 times per week[1]
- Administer Parsabiv® by intravenous bolus injection into the venous line of the dialysis circuit at the end of the hemodialysis treatment during rinse back or IV after rinse back[1]

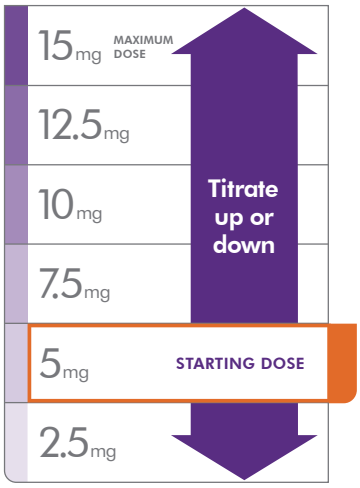
*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Only Parsabiv® offer flexible dosing that you control with IV administration[1]

Lab monitoring during Parsabiv® treatment

	PTH	Corrected Serum Calcium
Lab measurements after initiation or dose adjustment	after 4 weeks	at 1 week
Lab measurements once maintenance dose is established	per clinical practice	every 4 weeks

Titrate up or down as needed based on PTH and corrected serum calcium



Titrating up:

- Increase the dose of Parsabiv® in 2.5 mg or 5 mg increments until PTH is within recommended target range and corrected serum calcium is within normal range
- Increase no more frequently than every 4 weeks up to a maximum dose of 15 mg three times per week

Titrating down:

- Decrease or temporarily discontinue Parsabiv® when PTH is below target range
- Consider decreasing or temporarily discontinuing Parsabiv®,or use concomitant therapies,* when corrected serum calcium is below lower limit of normal† but > 7.5 mg/dL without symptoms of hypocalcemia

Reinitiating Parsabiv®:

- If dose is stopped, reinitiate Parsabiv® at a lower dose when PTH is within target range and hypocalcemia has been corrected

* Concomitant therapies include calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration.
† Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Managing calcium in patients taking Parsabiv®[1]

≥ 8.3 mg /dl*

Initiate Parsabiv®

- Do not initiate Parsabiv® if corrected serum calcium is less than the lower limit of normal*
- **Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv®.**Educate patients on the symptoms of hypocalcemia and advise them to contacta healthcare provider if they occur

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< 8.3 mg/dL to ≥ 7.5 mg/dL* without symptoms of hypocalcemia

Adjust Treatment as Needed

- **Consider decreasing or temporarily discontinuing Parsabiv® or use concomitant therapies to increase corrected serum calcium** (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration)

< 7.5 mg/dL or with symptoms of hypocalcemia

Withhold Parsabiv® an Monitor

- **Stop Parsabiv® and treat hypocalcemia**
- **Start or increase calcium supplementation** (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration)

- Throughout the studies, dialysate calcium concentration could be adjusted but had to remain ≥2 2.25 mEq/L[1]
- Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and entricular arrhythmias[1]

When cCa returns ≥ 8.3 mg/dl* —

Reinitiate Parsabiv®

- When corrected serum calcium levels cire within normal limits, symptoms of hypocalcemia have resolved, and predisposing factors for hypocalcemia have been addressed, reinitiate Parsabiv® at a dose 5 mg lower than the last administered dose. If patient's last administered dose of Parsabiv® was 2.5 mg or 5 mg, reinitiate at a dose of 2.5 mg

* Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

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(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Parsabiv (etelcalcetide)

Brief Prescribing Information. ▼This medicinal product is subject to additional monitoring. Please refer to the Summary of Product Characteristics before prescribing Parsabiv. **Pharmaceutical Form:** each vial contains 2.5 mg,5mg & 10mg etelcalcetide Solution for injection. **Indications:** Parsabiv is indicated for the treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy. **Posology and method of administration:** Posology: The recommended initial dose of etelcalcetide is 5 mg administered by bolus injection 3 times per week. Corrected serum calcium should be at or above the lower limit of the normal range prior to administration of first dose of Parsabiv, a dose increase, or reinitiation after a dose stop. Parsabiv should not be administered more frequently than 3 times per week. *Dose titration* Parsabiv should be titrated so that doses are individualised between 2.5 mg and 15 mg. The dose may be increased in 2.5 mg or 5 mg increments no more frequently than every 4 weeks to a maximum dose of 15 mg 3 times per week to achieve the desired parathyroid hormone (PTH) target. *Dose adjustments based on PTH levels* PTH should be measured after 4 weeks from initiation or dose adjustment of Parsabiv, and approximately every 1-3 months during maintenance. Dose adjustment may be necessary at any time during treatment including the maintenance phase. If PTH is below 100 pg/mL (10.6 pmol/L), the dose should be reduced or temporarily stopped. If PTH does not return to > 100 pg/mL following dose reduction, the dose should be stopped. For patients in whom the dose is stopped, Parsabiv should be reinitiated at a lower dose once PTH returns to > 150 pg/mL (15.9 pmol/L) and pre-dialysis serum corrected calcium (cCa) ≥ 8.3 mg/dL (2.08 mmol/L). If the patient's last administered dose was 2.5 mg, Parsabiv may be reinitiated at the 2.5 mg dose level if PTH is > 300 pg/mL (31.8 pmol/L), and the most recent pre-dialysis serum cCa ≥ 8.3 mg/dL (2.08 mmol/L). Additional recommendations related to the management of low calcium are provided in the table below. Parsabiv may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D sterols, as appropriate. *Missed doses* If a regularly scheduled haemodialysis treatment is missed, do not administer any missed doses. Parsabiv should be administered at the next haemodialysis treatment at the same dose. If doses are missed for more than 2 weeks, then Parsabiv should be administered at 5 mg, (or 2.5 mg if that was the patient's last administered dose) and titrated to achieve the desired PTH. *Dose adjustments based on serum calcium levels* Serum calcium should be measured within 1 week of initiation or dose adjustment of Parsabiv. Once the maintenance phase has been established for a patient, corrected serum calcium should be measured approximately every 4 weeks. In the studies total serum calcium was measured using Roche modular analysers. The lower limit of the normal range for corrected serum calcium was 8.3 mg/dL (2.08 mmol/L). Other laboratory assays may have different cut-offs for the lower limit of the normal range. In the event that clinically meaningful decreases in corrected serum calcium levels below the lower limit of the normal range occur and/or symptoms of hypocalcaemia occur, the following management is recommended: < 8.3 mg/dL (2.08 mmol/L) and ≥ 7.5 mg/dL (1.88 mmol/L) Recommendations: If clinically indicated: - start or increase calcium supplements, calciumcontaining phosphate binders, and/or vitamin D sterols. - increase dialysate calcium concentration. - consider reducing Parsabiv dose. < 7.5 mg/dL (1.88 mmol/L) or symptoms of hypocalcaemia recommendation: Stop Parsabiv until corrected serum calcium levels are ≥ 8.3 mg/dL (2.08 mmol/L) and symptoms of hypocalcaemia (if present) have resolved. If clinically indicated:- start or increase calcium supplements, calciumcontaining phosphate binders, and/or vitamin D sterols. - increase dialysate calcium concentration. Reinitiate Parsabiv at a dose 5 mg lower than the last administered dose. If patient's last administered dose was 2.5 mg or 5 mg, reinitiate at 2.5 mg once corrected serum calcium levels are ≥ 8.3 mg/dL (2.08 mmol/L) and symptoms of hypocalcaemia (if present) have resolved. Switch from cinacalcet to Parsabiv Parsabiv should not be initiated in patients until 7 days after the last dose of cinacalcet and the corrected serum calcium is at or above the lower limit of the normal range. *Paediatric population* The safety and efficacy of etelcalcetide in children and adolescents less than 18 years has not yet been established. No data are available. *Elderly* Dosing recommendations for elderly patients are the same as for adult patients. Method of administration: Parsabiv should not be diluted. Parenteral medicinal products should be inspected visually for particulate matter and change in colour prior to administration. Parsabiv is administered into the venous line of the dialysis circuit at the end of the haemodialysis treatment during rinse-back or intravenously after rinse-back. When given during rinse-back at least 150 mL of rinse-back volume should be administered after injection. If rinse-back is completed and Parsabiv was not administered, then it may be administered intravenously followed by at least 10 mL saline flush volume. **Contraindications** Hypersensitivity to the active substance or to any of the excipients listed. Parsabiv should not be initiated if corrected serum calcium is less than the lower limit of the normal range. **Special warnings and precautions for use** Hypocalcaemia Parsabiv treatment should not be initiated in patients if the corrected serum calcium is less than the lower limit of the normal range. Potential manifestations of hypocalcaemia include paraesthesias, myalgias, muscle spasm and seizures. Since etelcalcetide lowers serum calcium, patients should be advised to seek medical attention if they experience symptoms of hypocalcaemia and should be monitored for the occurrence of hypocalcaemia. Serum calcium levels should be measured prior to initiating treatment, within 1 week of initiation or dose adjustment of Parsabiv and every 4 weeks during treatment. If clinically meaningful decreases in corrected serum calcium levels occur, steps should be taken to increase serum calcium levels. Ventricular arrhythmia and QT prolongation secondary to hypocalcaemia Decreases in serum calcium can prolong the QT interval, potentially resulting in ventricular arrhythmia. Serum calcium levels should be closely monitored in patients with congenital long QT syndrome, previous history of QT prolongation, family history of long QT syndrome or sudden cardiac death and other conditions that predispose to QT prolongation and ventricular arrhythmia while being treated with Parsabiv. Convulsions Cases of seizures have been reported in patients treated with Parsabiv. The threshold for seizures may be lowered by significant reductions in serum calcium levels. Serum calcium levels should be closely monitored in patients with a history of a convulsion disorder while being treated with Parsabiv. *Worsening heart failure* Decreased myocardial performance, hypotension, and congestive heart failure (CHF) may be associated with significant reductions in serum calcium levels. Serum calcium levels should be monitored in patients with a history of congestive heart failure while being treated with Parsabiv, which may be associated with reductions in serum calcium levels. Co-administration with other medicinal products Administer Parsabiv with caution in patients receiving any other medicinal products known to lower serum calcium. Closely monitor serum calcium. Patients receiving Parsabiv should not be given cinacalcet. Concurrent administration may result in severe hypocalcaemia. Adynamic bone: Adynamic bone may develop if PTH levels are chronically suppressed below 100 pg/mL. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or Parsabiv should be reduced or therapy discontinued. After discontinuation, therapy can be resumed at a lower dose to maintain PTH in the target range. Immunogenicity In clinical studies, 7.1% of patients with SHPT treated with Parsabiv for up to 6 months tested positive for binding antibodies. 80.3% of these had pre-existing antibodies. No evidence of altered pharmacokinetic profile, clinical response or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide antibodies with a clinically significant effect is suspected, contact the Marketing Authorisation Holder to discuss antibody testing. Contact details are provided in section 6 of the package leaflet. Excipient with known effectParsabiv contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'. Interaction with other medicinal products and other forms of interaction No interaction studies have been performed. There is no known risk of pharmacokinetic interaction with etelcalcetide. In vitro, etelcalcetide did not inhibit or induce CYP450 enzymes and was itself not a substrate for metabolism by CYP450 enzymes. In vitro, etelcalcetide was not a substrate of efflux and uptake transporter proteins; and etelcalcetide was not an inhibitor of common transporter proteins. Concurrent administration of other medicinal products known to reduce serum calcium and Parsabiv may result in an increased risk of hypocalcaemia. Patients receiving Parsabiv should not be given cinacalcet. **Fertility, pregnancy and lactation** Pregnancy There are no or limited amount of data from the use of etelcalcetide in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Parsabiv during pregnancy. Breast-feeding It is unknown whether etelcalcetide is present in human milk. Available data in rats have shown that etelcalcetide is excreted in milk. A risk to breastfed newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or discontinue/abstain from Parsabiv therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Fertility No data are available on the effect of etelcalcetide on human fertility. Animal studies do not indicate direct or indirect harmful effects with respect to fertility. Effects on ability to drive and use machines Parsabiv has no or negligible influence on the ability to drive and use machines. However, certain potential manifestations of hypocalcaemia may affect the ability to drive and use machines. Undesirable effects: Very common (≥1/10): blood calcium decreased, muscle spasms, diarrhoea, nausea, and vomiting. Common (≥ 1/100 to < 1/10) Hypocalcaemia, hyperkalaemia, hypophosphatemia, Headache, Paraesthesia, worsening heart failure, QT prolongation, hypotension and Myalgia. Uncommon (≥ 1/1,000 to < 1/100): Convulsions. Side effects with unknown frequency: Hypersensitivity reactions (including anaphylaxis) **Overdose:** Overdose of etelcalcetide may lead to hypocalcaemia with or without clinical symptoms and may require treatment. In the event of overdose, serum calcium should be checked, and patients should be monitored for symptoms of hypocalcaemia and appropriate measures should be taken. Although Parsabiv is cleared by dialysis, haemodialysis has not been studied as a treatment for overdose. Single doses up to 60 mg and multiple doses up to 22.5 mg 3 times a week at the end of dialysis in patients receiving haemodialysis were safely administered in clinical trials. **Special precautions for storage:** Store in a refrigerator (2°C – 8°C). Keep the vial in the outer carton in order to protect from light. **Special precautions for disposal:** For single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements. **Legal Category:** POM. **Administrative information:** Date of PI: February 2019. **Marketing Authorisation Holder:** Amgen Europe B.V. Minervum 7061-4817 ZK Breda, The Netherlands. Registration number:Parsabiv 2.5mg (14360-16111-1), Parsabiv 5mg(14360-16111-2), Parsabiv 10mg(14360-16111-3). **Local representative in UAE:** City Pharmacy. Address: Al Otaiba Towers, 9th floor Flat 901 SH. Hamdan St. Abu Dhabi P.O. Box 2098. Tel: 00971 26323016 Ext. 230.

Any suspected adverse reactions should be reported immediately to City Pharmacy and/or Amgen in accordance with local spontaneous reporting requirements. Amgen Global Fax: 0044 2071361046 or send to AGS mailbox: svc-ags-in-uk@amgen.com and Safety-MEA@amgen.com

For any questions or additional information please contact Amgen Medical Information @ meamedinfo@amgen.com

References

1. Parsabiv® Smpc revision Feb 19, Amgen
2. Block GA, Bushinsky DA, Cunningham J, et al. Effect of etelcalcetide vs placebo on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: two randomized clinical trials. JAMA. 2017;317:146-155.

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AMGEN®

Amgen Middle East FZZ-LC
Business Central Tower building A, Office 2007.
P.O. Box 502607, Dubai Media City, Dubai, UAE.