## Report KISPLYX® lenvatinib - RCC

Brand Name: Kisplyx  Originator/Ilcensee: Eisal GC in combination with advanced RCC and no previous systems therapy. Pis were enrolled regardless of PO-1.1 tumor expression of CC in combination with permbrolizumab, as first-line treatment [2].  Classification: NI  ATC code: L01EX08  Orphan Status: the first line treatment of adult pts with advanced RCC [3]  Orphan Status: the first line treatment of adult pts with advanced RCC [3]  Orphan Status: the first line treatment of adult pts with advanced RCC [1]  Route of administration: OS  Us:   Mechanism of action: Leuvatinib is a RTK inhibitor that selectively inhibits the activities of VeCFF receptor's kinase VEGFR2, and VECFF and PCFC [3]  Classification is a RTK inhibitor that selectively inhibits the activities of VeCFF receptor's kinase VEGFR2 and VECFF real possible of the promote of the permonent of the per	Product &	Authorized indications	Essential therapeutic features	NHS impact
EMA: I envirtinib is indicated for the retartment of adult pts with advanced RCC and no provided RCC and n	Mechanism of action	Licensing status		
Originator/licensee: Eisal GmbH  Classification: NI  Classification: NI  FDA: Inevatinib is indicated, combination with pembrolizumab, as first line treatment of adulty for wheest benefit of RECLET 1, and OS.  ATC code: LOIEXOR  FDA: Inevatinib is indicated, in combination with pembrolizumab, in first line retentment of adulty for wheest benefit of RECLET 1, and OS.  ATC code: LOIEXOR  FDA: Inevatinib is indicated, in combination with pembrolizumab, for the first line retentment of adulty for wheest benefit of RECLET 1, and OS.  Bus:  Classification: NI  Mechanism of action:  Lenvatinib art RIX inhibitor that selectively inhibits the activities of VEGF receptor RIX. related to promoting the receptor of the selection of the receptor wheeling in the selection of	Substance: lenvatinib		•	Cost of therapy: In Italy, the cost of lenvatinib is 1,692.07 € for
Organizor/Incensee: Estal   Growth   Factor   Freedom	Brand Name: Kisplyx	·	status. Pts were randomized to receive:	30 capsules (10 mg) (ex-factory price) [6] One-month treatment costs 3,384.14 € (the
Classification: NI  ATC code: LO1EX08  Orphan Status: Eu: No Us:   Mechanism of action: Levatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR2 and VEGFR2 and Selectively inhibits the activities of VEGF receptor kinase VEGFR2 and VEGFR2 and November of Commentation of Comm		The state of the s	• n=357, lenvatinib 18 mg orally daily + everolimus 5 mg orally daily	recommended dose of lenvatinib is 20 mg orally once daily) [1].
ATC code: LOIEX08  Orphan Status:  Eu: No  Us: -  Mechanism of action: Lenvatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor Kinase VEGFR3, and addition to other RTKs related to prorangiogenic and oncogenic agents, including FGF receptors FGFR2, 2, 3, 4, PDGFR0, KIT and RET [1].  **PDGFR0, KIT and RET [	Classification: NI	FDA: lenvatinib is indicated, in	Treatment continued until unacceptable toxicity or disease progression.	, ,
Orphan Status:  Eur. No Us:  Mechanism of action: Leonatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1, VEGFR2 and VEGFR3, in addition to other RTKs related to proanglogenic and oncogenic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRQ, KIT and RET [1].  **Mechanism of action: Leonatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1, VEGFR2 and VEGFR3, and addition to other RTKs related to proanglogenic and oncogenic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRQ, KIT and RET [1].  **Memoritation of the Committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation Metalata Receptor Nitic Humanu bear Memoritation of the committee for Medicinal Products for Humanu bear Memoritation (55.4%, 45.6%, 41.5%), hypothyroidism (47.2%, 26.8%, 26.5%) [3-5].  **PGF receptors FGFR1, 2, 3, 4, PDG-FRQ, KIT and RET [1].  **PDE-TROGRAMMIC Comments for Medicinal Products for Humanu bear Memoritation Metalata Receptor Alpha PRS Progression for committee for Medicinal Products for Humanu bear Memoritation Metalata Receptor Alpha PRS Progression for committee for Medicinal Products for Humanu bear Memoritation Metalata Receptor Alpha PRS Progression for committee for Medicinal Prod	ATC code: L01EX08	•	95% CI: 0.32 to 0.49; p<0.001); median PFS was 14.7 months in the lenvatinib +everolimus arm vs. 9.2 months in	were 13,521. In about 25-30% of pts it occurs
Eu: No US:  Mechanism of action: Lenvatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1, VEGFR2 and VEGFR3, in addition to othe RTKs related to proangiogenic and oncogenic gents, including FGF receptors FGFR1, 2, 3, 4, PDGFRa, KIT and RET [1].  DGFRa, KIT generated  DGFRa, Entertherion-  GG. Overall Survival  DGFRa, Entertherion-  GGC. Renal Cell Cardinoma  MCCST v.L. Response Fouldation Criteria in Solid Tumors  MCCST v.L.	Orphan Status:	advanced RCC.[1]	$Survival\ rate\ at\ 24\ months\ was:\ 79.2\%\ in\ the\ lenvatinib+pembrolizumab\ arm\ vs.\ 66.1\%\ in\ the\ lenvatinib+everolimus$	,
Mechanism of action: Lenvalinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1, VEGFR and VEGFR3, and addition to other RTKs related to proangiogenic and oncogenic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRa, KIT and RET [1].  **BOAGRAM RET [1].**  **BOAGRAM RET [1].*  **BOAGRAM RET [1].**  **BOA		Route of administration: OS	OS was longer with lenvatinib + pembrolizumab than with sunitinib (HR: $0.66$ ; $95\%$ CI: $0.49$ to $0.88$ ; p = $0.005$ ). OS	
Lenvatinib is a RIK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1, VEGFR2 and VEGFR3, in addition to other RTKs related to proangiogenic and oncogenic agents, including FGF receptor SFGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  Horizontal Residual	Mechanism of action:		•	options are the following: sunitinib; pazopanib;
activities of VEGFR2 and knase VEGFR1, VEGFR2 and VEGFR3, in addition to other RTKs related to proangiogenic and conception and conception and conception and conception and conception and provided in the sunitinib arm. SAEs included in the three arms, respectively; hypertension (2.27%, 0.56%, 0.59%), acute kidney injury (2.27%, 2.82%, 1.47%), adrenal insufficiency (2%, 0%, 0%) and myocardial infarction (1.70%, 0.85%, 49.4%), hypertension (2.27%, 0.56%, 0.59%), acute kidney injury (2.27%, 2.82%, 1.47%), adrenal insufficiency (2%, 0%, 0%) and myocardial infarction (1.70%, 0.85%, 49.4%), hypertension (2.27%, 0.56%, 0.59%), acute kidney injury (2.27%, 2.82%, 1.47%), adrenal insufficiency (2%, 0%, 0%) and myocardial infarction (1.70%, 0.85%, 49.4%), hypertension (2.27%, 0.56%, 0.59%), acute kidney injury (2.27%, 2.82%, 1.47%), adrenal insufficiency (2%, 0%, 0%) and myocardial infarction (1.70%, 0.85%, 49.4%), hypertension (2.27%, 0.56%, 0.59%), acute kidney injury (2.27%, 0.56%, 0.56%, 0.56%, 0.59%), acute kidney injury (2.27%, 0.56	that selectively inhibits the	, ,	lenvatinib+everolimus arm and 98.5% in sunitinib arm). Serious AEs occurred in 50.57% of the pts in the	(indicated in pts with intermediate-
## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## DGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## ABBREWATIONS: AE: Adverse Events Organic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  ## Abbrewation Fine Agents of the Abbrewation For the Abbrewation For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abbrewation For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N Engl J Med. Declaration For Abranical Renal Cell Carcinoma, N E			in the sunitinib arm. SAEs included in the three arms, respectively: hypertension (2.27%, 0.56%, 0.59%), acute	IMDC, only); bevacizumab + IFN- $\alpha$ and
CHMP: Commettee for Medicinal Products for Human Use of Efficitionists growth factor Receptor Fifer Fith 2, 3, 4, 4, PDGFRα, KIT and RET [1].   PDGFRα independent Radiologic Review Max. Marketing Authorization MSKC: Memorial Soan Kettering Cancer Center OS: Overall Survival p. p-value PDGFRα: Floral Survival p. p-value PGGFRα: Floral Survival p. p-value PGGFRα: Floral Survival p. p-va	RTKs related to	ABBREVIATIONS:	0.29%). The most common non-serious in the three groups were, respectively: diarrhea (61.4%, 66.5%, 49.4%),	with unfavorable risk according to MSKCC
FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].  HR: Hazard Ratio KIT: stem cell factor receptor IMDC: International Metastatic Renal Cell Carcinoma Database Consortium INF-α: Interferon-α IRC: Independent Radiologic Review MA: Marketing Authorization MSKCC: Memorial Sloan Kettering Cancer Center OS: Overall Survival p: p-value PDGFRα: Platelet Derived Growth Factor Receptor Alpha PPS: Progression free survival PD-11: Programmed Cell Death-1 PD-12: Programmed Cell Death-1 PD-12: Programmed Cell Death-1 PD-12: Programmed Cell Death-1 PD-13: patients RCC: Renal Cell Carcinoma RCCST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. RET: rearranged during transfection protein receptor RTC. Tyrosine Kinase Receptor or RTC. Tyrosine	oncogenic agents, including	FGF: fibroblast growth factor		,,,,,
Discontinued studies (for the same indication): No  IRC: Independent Radiologic Review MA: Marketing Authorization MSKCC: Memorial Sloan Kettering Cancer Center OS: Overall Survival p: p-value PDGFRa: Platelet Derived Growth Factor Receptor Alpha PFS: Progression free survival PD-1: Programmed Cell Death-1 PD-1: Programmed Cell Death-		HR: Hazard Ratio KIT: stem cell factor receptor		
MA: Marketing Authorization MSKCC: Memorial Sloan Kettering Cancer Center OS: Overall Survival p: p-value PDGFRa: Platelet Derived Growth Factor Receptor Alpha PFS: Progression free survival PD-1: Programmed Cell Death-1 PD-1: Programmed Cell Death-1 PO: Positive Opinion pts: patients RCC: Renal Cell Carcinoma RCCIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. RET: rearranged during transfection protein receptor RTK: Tyrosine Kinase Receptor  MA: Marketing Authorization MSKCC: Memorial Sloan Kettering Cancer Center OS: Overall Survival p: p-value p-p-value p-p-tale to Derived Growth Factor Receptor Alpha pFS: Progression free survival p-p-1: Programmed Cell Death-1 p-1: Programmed Cell Death-1 po: Positive Opinion pts: patients RCC: Renal Cell Carcinoma RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. RET: rearranged during transfection protein receptor RTK: Tyrosine Kinase Receptor  Masketting Authorization References:  1. https://www.aiom.it/wp-content/uploads/2020/10/2020 Numeri Cancro-operatori_web.pdf Notice References:  2. https://www.aiom.it/wp-content/uploads/2020/10/2020 Numeri Cancro-operatori_web.pdf Notice References:  3. https://www.aiom.it/wp-content/uploads/2020/10/2020 Numeri Cancro-operatori_web.pdf Notice References:  5. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. 2021;384(14):1289-1300. doi:10.1056/NEIMoa2035716 6. https://gallery.farmadati.it/home.aspx 7. https://www.aiom.it/wp-content/uploads/2020/10/2020 Numeri Cancro-operatori_web.pdf Notice References:  Notice References:  1. https://www.eaceuropa.eu/en/medicines/human/summaries-opinion/keytruda-5 Notice References:  2. https://www.eaceuropa.eu/en/medicines/human/summaries-opinion/keytruda-5 Notice References:  3. https://www.aiom.aic.pop/ct2/fesults/NCT0288118612term=NCT028118613term=NCT028118613term=NCT028118613term=NCT028118613term=NCT028118613term=NCT028118613term=NCT028118613term=NCT028118613term=NCT0281186		Database Consortium INF- $\alpha$ : Interferon- $\alpha$	Discontinued studies (for the same indication): No	thyroid cancer, head and neck squamous cell carcinoma, malignant melanoma, non-small
p: p-value PDGFRa: Platelet Derived Growth Factor Receptor Alpha PPS: Progression free survival Pp-1: Programmed Cell Death-1 Pp-1: Programmed Cell Death-Uignad1 Pp-1: Programmed Cell Death-Uignad2 Pp-1: Programmed Cell Death-Uignad2 Pp-1: Programmed Cell Carcinoma. N Engl J Med. Pp		MA: Marketing Authorization MSKCC: Memorial Sloan Kettering Cancer Center	References:	cell lung cancer, urothelial carcinoma, endometrial neoplasms and other [9]
PD-1: Programmed Cell Death-1 5. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. PD-1: Programmed Cell Death-Ligand1 PD: Postitive Opinion pts: patients RCC: Renal Cell Carcinoma RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. RET: rearranged during transfection protein receptor RTK: Tyrosine Kinase Receptor  Notzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716 6. https://gallery.farmadati.it/Home.aspx 7. https://www.aiom.it/wp-content/uploads/2020/10/2020_Numeri_Cancro-operatori_web.pdf 8. https://www.aiom.it/wp-content/uploads/2021/04/2020_LG_AIOM_Rene.pdf 9. https://clinicaltrials.gov/ct2/results?cond=&term=&type=intr&rsit=&recrs=b&recrs=d&age_v=&gndr=&intr=Pe_mbrolizumabk.titles=&content_operatori_web.pdf Tivozanib+Nivolumab, Nivolumab+Ipilimu bempegaldesleukin, Atezolizu prod e=&sfpd s=&sfpd s=&sfpd s=&sfpd s=&sfpd s=&slupd s=&lupd s=&lupd s=&lupd s=&slupd s=&slupd s=&surd= Sorafenib+Pazopanib, Dovitinib [10]		p: p-value PDGFRa: Platelet Derived Growth Factor Receptor Alpha	<ol> <li>https://www.ema.europa.eu/en/medicines/human/summaries-opinion/keytruda-5</li> <li>https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s102lbl.pdf</li> </ol>	SAME INDICATION IN EARLIER LINE(S) OF
pts: patients RCC: Renal Cell Carcinoma RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. RET: rearranged during transfection protein receptor RTK: Tyrosine Kinase Receptor  ### Tivozanib A in the string of the string o		PD-1: Programmed Cell Death-1 PD-11: Programmed Cell Death-Ligand1	5. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med.	
9. https://clinicaltrials.gov/ct2/results?cond=&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=Pe_mbrolizumab&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsub=&strd_e=&prcd_s=&prcd_e=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&lipd_s=&lipd_e=&sort=		pts: patients RCC: Renal Cell Carcinoma	7. https://www.aiom.it/wp-content/uploads/2020/10/2020_Numeri_Cancro-operatori_web.pdf	SAME INDICATION: sorafenib, Pazopanib,
The Tytosine kindse neceptor		version 1.1.  RET: rearranged during transfection protein receptor	9.https://clinicaltrials.gov/ct2/results?cond=&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=Pe_mbrolizumab&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsub=&strd_s=&strd_e=∏_s=&	bempegaldesleukin, Atezolizumab,
VEGF: Vascular Endothelial Growth Factor     d&recrs=e&recrs=f&type=intr&phase=2     *Service reorganization No		SAE: serious AE	10.https://clinicaltrials.gov/ct2/results?cond=Renal+Cell+Carcinoma&term=&cntry=&state=&city=&dist=&recrs=a&recrs=b&recrs=	
VEGFR: Vascular Endothelial Growth Factor Receptor vs.: versus  VEGFR: Vascular Endothelial Growth Factor Receptor vs.: versus  *Possible off label use Yes		VEGFR: Vascular Endothelial Growth Factor Receptor		_