New Therapy to Treat Advanced Small Cell Lung Cancer ZEPZELCA® (lurbinectedin) Approved in Singapore

Singapore, 22 September 2021: SINGAPORE patients with an aggressive form of lung cancer (metastatic small cell cung cancer) can now access a new therapy that may improve outcomes.

The drug ZEPZELCA (lurbinectedin) has been provisionally approved by Singapore's Health Sciences Authority (HSA) "**for the treatment of adult patients with metastatic small cell lung cancer (SCLC) who have progressed after prior platinum-containing chemotherapy".**[1]

This means patients who have failed other existing treatment options will now have a further therapeutic option.

ZEPZELCA is the first new therapy approved by the HSA to treat second-line SCLC in more than two decades, and is the third oncology drug in Specialised Therapeutics (ST) portfolio to receive HSA approval.

The Singapore approval follows on from approvals by the US Food and Drug Administration (FDA) decision[2], as well as the Therapeutic Goods Administration (TGA) in Australia.[3]

"The new availability of ZEPZELCA will be welcomed by patients, families and the medical community, as we strive to improve patient outcomes for this disease," Professor Mitchell said.

"With this approval, we now have another option for patients who have progressed after prior platinum-based treatments. This provides an opportunity for them to continue treatment and potentially, improve outcomes."

The HSA approval of ZEPZELCA has been granted following collaboration with the US FDA via the 'Project Orbis' initiative, due to the high unmet clinical need

in SCLC. It is based on monotherapy clinical data from an open-label, multi-centre, single-arm study in 105 adult platinum-sensitive and platinum-resistant patients with SCLC who had disease progression after treatment with platinum-based chemotherapy.[6]

The data, which appeared in *The Lancet Oncology* May 2020 issue, demonstrated that in patients with relapsed SCLC, ZEPZELCA provided an ORR of 35% and a median duration of response of 5.3 months as measured by investigator assessment (30% and 5.1 months respectively, as measured by an independent review committee (IRC)).[6]

The provisional approval is the subject of a further confirmatory study in more than 700 patients with 2L SCLC. This study is expected to be completed in 2025.

ZEPZELCA is being made available in Singapore by independent pharmaceutical company Specialised Therapeutics under exclusive license from its international partner PharmaMar.

Specialised Therapeutics Chief Executive Officer Mr Carlo Montagner said lung cancer was the third most common cancer in Singapore, representing more than 22% of all cancer deaths. SCLC represented between 10 – 15% per cent of all lung cancer diagnoses.[7,8]

“We are delighted to be able to provide a new therapy option in Singapore for patients with this difficult to treat cancer,” he said.

“While patients may initially respond to traditional chemotherapy, they often experience an aggressive recurrence that is historically resistant to treatment.

“We expect that this therapy may now be an option for up to 100 Singapore patients every year and look forward to making a difference for these patients and their families.”

PharmaMar president José María Fernández Sousa-Faro, PhD, said the company was delighted South-East Asian patients would now be provided access to ZEPZELCA.

“We are pleased to bring a new treatment choice to relapsed SCLC patients. “The accelerated approval of ZEPZELCA underscores its potential to fill an unmet

need in this often-overlooked SCLC community."

ZEPZELCA has been available in Singapore via an Early Access Program since July 2020.

Ends.

About SCLC in Singapore

SCLC represents a serious condition. It is a particularly aggressive type of lung cancer related to smoking that represents approximately 10-15% of all lung cancers, accounting for more than 275,000 new cases worldwide every year.[9,10] SCLC is characterised by rapid growth, early dissemination that is often asymptomatic and with acquired resistance to drugs. SCLC is staged into limited-stage or extensive-stage disease. Limited-stage disease is potentially curable with aggressive therapy consisting of concurrent chemoradiotherapy, prophylactic cranial irradiation, and occasionally, surgery.[11,12] However, nearly two-thirds of SCLC patients have extensive-stage disease at diagnosis, which is not curable, and patients are treated with palliative intent, with a median survival of 7 to 11 months after diagnosis and with less than 5% survival at 2 years.[13,14]

Lung cancer is the third most common cancer in Singapore and represents 22.3% of all cancer deaths. Between 2014 and 2018, approximately 7,945 new cases of lung cancer were diagnosed in Singapore, with 10-15% of these classified as SCLC (between 150 and 240 new SCLC cases annually).7,8 While the age-standardised incidence rate of all lung cancer has been in decline since the 1970's (mid-50's per 100,000 in 1968 to mid-30's per 100,000 in 2017), the five-year relative survival has seen a moderate increase to approximately 10% in 2017. Globally, the prognosis of patients with SCLC is dismal with a 5-year survival rate of less than 5% and an average overall survival period of only 2–4 months for patients not receiving any active treatment.[11,12]

Modern studies, including those of recent immunotherapies, suggest that between 40-60% of patients that receive front-line therapy will be clinically

eligible for second-line therapy.[15-18] This suggests that, based on 2014-2018 lung cancer incidence figures from the Singapore Cancer registry8, between 60 to 100 patients would be eligible for second-line SCLC treatment in Singapore.

About ZEPZELCA® (lurbinectedin)

ZEPZELCA is an alkylating drug that binds guanine residues within DNA. This triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and eventual cell death.[1]

ZEPZELCA or injection 4 mg is a prescription medicine used to treat adults with a kind of lung cancer called small cell lung cancer (SCLC) that has spread to other parts of the body (metastatic) and who have received treatment with chemotherapy that contains platinum, and it did not work or is no longer working. ZEPZELCA is approved based on response rate and how long the response lasted. Additional studies will further evaluate the benefit of ZEPZELCA for this use.

About the Phase II Monotherapy Trial

The Phase 2 trial of ZEPZELCA was an open-label, single-arm study, which enrolled a total of 105 SCLC patients at 26 hospitals in six European countries and the U.S.[6] In the trial, platinum-sensitive and platinum-resistant patients were treated with ZEPZELCA 3.2 mg/m^2, administered as a 60-minute IV infusion repeated every 21 days until disease progression or unacceptable toxicity. The primary endpoint, ORR, was 35% and the median duration of response was 5.3 months as measured by investigator assessment (30% and 5.1 months respectively, as measured by an IRC).[6] ZEPZELCA was discontinued in 1.9% of patients and was delayed in 30.5% of patients due to an adverse reaction. Dose reductions for an adverse reaction occurred in 25% of patients.[6]

About Specialised Therapeutics Asia

Headquartered in Singapore, Specialised Therapeutics Asia Pte Ltd (STA) is an international biopharmaceutical company established to commercialise new

therapies and technologies to patients throughout South East Asia, as well as in Australia and New Zealand. STA and its regional affiliates collaborate with leading global pharmaceutical and diagnostic companies to bring novel, innovative and life-changing healthcare solutions to patients affected by a range of diseases. Its mission is to provide therapies where there is an unmet need. The company's broad therapeutic portfolio currently includes novel agents in oncology, haematology, neurology, ophthalmology and supportive care. Additional information can be found at www.stbiopharma.com

About PharmaMar

Headquartered in Madrid, PharmaMar is a biopharmaceutical company, focused on oncology and committed to research and development which takes its inspiration from the sea to discover molecules with antitumor activity. It is a company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. Its commitment to patients and to research has made it one of the world leaders in the discovery of antitumor drugs of marine origin.

PharmaMar has a pipeline of drug candidates and a robust R&D oncology program. It develops and commercializes YONDELIS® in Europe and has other clinical-stage programs under development for several types of solid cancers: lurbinectedin (PM1183), PM184 and PM14. With subsidiaries in Germany, Italy, France, Switzerland, Belgium, Austria and the United States. PharmaMar wholly owns other companies: GENOMICA, a molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi). To learn more about PharmaMar, please visit us at www.pharmamar.com.

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