1 Synopsis

Name of Sponsor/Company: Pharmazeutische Fabrik Montavit Ges.m.b.H. Salzbergstraße 96, A-6067 Absam, Austria	**EudraCT number: 2013-004836-31**
Name of finished product: Tavipec® capsules with gastroresistant coating	
Name of active ingredient: Spicae aetheroleum	

Title of study:	Double-blind, randomized, placebo-controlled study evaluating the Efficacy and Safety of Tavipec® capsules in acute Bronchitis
Study centres:	*3 study centers in Austria* 101 Prof. Dr. Christian Kähler, Anichstraße 35, Internal Medicine VI, Pneumology, Medical University of Innsbruck, 6020 Innsbruck 102 Dr. Andrea Keckeis, Werdenberger Straße 26, 6700 Bludenz 103 Dr. Sensoy Muhammed Ali; Dr.-Waibel-Straße 1b, 6850 Dornbirn *5 study centers in Poland* 201 Derenzinski Tadeuz, MD, PhD; 688-140 Gniewkowo, Dworcowa 8 202 Bocian-Sobkowska, MD, PhD; 60-185 Skorzewo, Poznanska 74 203 Filipczak Robert, MD, PhD; 96-200 Rawa Mazowiecka, Krakowska 9 204 Wisniewska Dorota, MD, PhD; 87-100 Torun, Szczytna 20 205 Kubalski Piotr, MD, PhD; 86-300 Grudziadz, Poniatowskiego 15
Phase of development:	IV
Study (treatment) period:	May 2014 – January 2016
Objectives:	In terms of efficacy: o Evaluation of effects on relevant symptoms, incl.coughing, sputum, rales/rhonchi, chest pain during coughing, dyspnea. In terms of impact of disease on quality of life (QoL) from patients´ view: o Evaluation of change of QoL by global assessment (verbal rating) scale. In terms of safety and tolerance: o Evaluation of side effects (incidence and severity).
Methodology:	Prospective, multi-centre, parallel group, interventional clinical phase IV study
Number of patients:	Enrolled: 269 patients Evaluable for safety analysis: 258 patients Evaluable for efficacy analysis (primary endpoint): 245 ITT/229 PP patients
Diagnosis and main criteria for inclusion:	Patients aged between ≥18 and 75 years who present with acute bronchitis.
Test product:	Tavipec® capsules with gastroresistant coating
Dose:	2 capsules containing 150 mg spicae aetheroleum each, thrice daily
Mode of admin.:	Oral
Batch number(s):	13449501; Expiry 05/2018
Placebo:	Placebo capsules with gastroresistant coating
Dose:	2 capsules containing Medium-Chain Triglycerides each, thrice daily
Mode of admin.:	Oral
Batch number(s):	11536401(Expiry 02/2015, prolonged to 31.12.2016)
Duration of treatment:	10 days

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Criteria for evaluation:

Efficacy:

Primary:

- Mean difference of a defined total bronchitis severity score (BSS) of 25% between the verum group and the placebo group after 7 days of full medication dose.

Secondary:

- Mean difference of a defined total BSS of 25% between the verum group and the placebo group after 10 days of full medication dose.
- Global impact of disease on QoL as assessed by patient after 7 and 10 days of full medication dose.

Safety: Adverse event rate.

Statistical methods:
Primary endpoint: Mann-Whitney test
Secondary endpoints: Mann-Whitney test; descriptive statistical methods
Safety analysis: Descriptive statistical methods

SUMMARY – CONCLUSIONS:
Efficacy results:

PRIMARY EFFICACY EVALUATION
BSS: Mean change (improvement from baseline) at day 7, ITT/PP

	Tavipec	**Placebo**	**Tavipec**	**Placebo**
	ITT		**PP**	
Mean	4.53	2.92	4.79	3.2
Number of patients	125	120	119	110
Significance	**<0.001**		**<0.001**	

SECONDARY EFFICACY EVALUATION
BSS: Mean change (improvement from baseline) at day 10, PP

	Tavipec	**Placebo**
Mean	6.47	4.32
Number of patients	119	110

QoL score: Mean change (improvement from baseline) at day 7 and day 10, ITT

	Day 7		**Day 10**	
	Tavipec	**Placebo**	**Tavipec**	**Placebo**
Mean	4.5	2.9	6.52	4.46
Number of patients	125	120	119	112

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SUMMARY – CONCLUSIONS (continued):
Safety results:

22 out of 258 patients (13/131 group Tavipec, 9/127 group Placebo) reported a total number of 27 adverse events (15 group Tavipec, 12 group Placebo).
Drug-related AEs were experienced by 10/131 patients in the Tavipec group (7.6%) and 5/127 patients in the Placebo group (3.9%), including gastrointestinal disorders (10 in the Tavipec group; 5 in the Placebo group), skin and subcutaneous tissue disorders and respiratory, thoracic and mediastinal disorders (1 each in the Tavipec group).
One serious unrelated AE was reported in the Placebo group.

Conclusions:

Assessment of the Bronchitis Severity Score
During a 7-day treatment course the BSS improved by a mean of 4.53 and 2.92 score points in the Tavipec and Placebo group, respectively in the ITT population, and by a mean of 4.79 and 3.2 score points, respectively in the PP population, resulting in a difference between both groups in terms of improvement of 1.6 score points (ITT: 1.61, PP: 1.59).
After 10-days treatment, the improvement of the BSS between Tavipec and Placebo differed by 2.15 score points (Tavipec: 6.47, Placebo: 4.32).
As confirmed with the Mann-Whitney test the BSS for the Tavipec group was significantly lower than for the Placebo group at both, day 7 and day 10 ($p<0.001$).

Assessment of quality of life with verbal rating scale
The improvement of quality of life was significantly in favour of Tavipec.
The proportion of patients reporting only a mild impact of disease on quality of life at baseline, day 7, and day 10 was 0.8%, 62.4%, and 94.1%, respectively in the Tavipec group and 0%, 28.3%, and 51.8%, respectively in the Placebo group.

The presented study provides no new information with respect of any safety related concern.
Adverse events such as gastrointestinal tract reactions and hypersensitivity reactions are known adverse drug reactions of Tavipec capsules and listed in the SmPC.

Date of the report: 14 June 2016