Swiss Summary of the Risk Management Plan (RMP)

for Aklief (Trifarotene)

Based on the EU RMP Aklief (Trifarotene) ver1.3 dated 09-Dec-2019, with Data Lock Point 14-Mar-2018

Active substance(s) (INN or common name):	Trifarotene
Product(s) concerned (brand name(s)):	AKLIEF®
Name of Marketing Authorisation Holder or Applicant:	GALDERMA SA Zählerweg 10, 6300 Zug, Switzerland
Swiss Summary RMP Version	1.0
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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The Swiss RMP summary of Aklief® (trifarotene) is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Aklief® (trifarotene) in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Galderma SA is fully responsible for the accuracy and correctness of the content of the published summary RMP of Aklief®.

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Part VI: Summary of the risk management plan

This is a summary of the risk management plan (RMP) for Aklief. The RMP details important risks of Aklief, how these risks can be minimised, and how more information will be obtained about Aklief's risks and uncertainties (missing information). Aklief's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Aklief should be used.

I. The medicine and what it is used for

Aklief is authorised for the cutaneous treatment of Acne Vulgaris of the face and/or the trunk in patients from 12 years of age and older, when many comedones, papules and pustules are present (see SmPC for the full indication). It contains trifarotene as the active substance and it is given by cutaneous route.

Overview of disease epidemiology

Indication: Acne Vulgaris

The targeted indication for trifarotene 50 µg/g cream is the topical treatment of acne vulgaris of the face and/or trunk in patients 12 years of age and older, when many comedones, papules and pustules are present.

Incidence:

Acne vulgaris is one of the most common dermatological diseases, affecting an estimated 85% of teenagers, and often continues into adulthood. Although onset of acne normally begins in adolescence, it is not uncommon for individuals to experience their first symptoms after puberty, with

30-40% of cases reportedly occurring between the ages of 35–45. Acne affects approximately 650 million people worldwide, or nearly 1 in every 10 people.

Prevalence:

Acne is one of the most prevalent inflammatory skin diseases. Over the past 15 years, various general population prevalence studies on acne have been conducted. The largest of these community-based studies in which participants were examined by dermatologists were performed in China (n = 17 345), Germany (n = 90 880) and Egypt (n = 8008). Despite the geographical and temporal dispersion of these studies, the prevalence of acne was consistent, with point prevalence rates of 8.1%, 3.9% and 5.4 %, respectively. These studies also provided evidence on the peak age (or age range) of acne, putting it within the age range of 16–20 years.

Epidemiological data have disclosed that, on a global scale, it is the eighth most frequent disease, with 9.4% predominance, including both adults and adolescents of several ethnic groups. Acne vulgaris, or acne of the adolescent, has a peak incidence in 14- and 17-year-old girls and in 16- and 19-year-old boys.

There is very limited literature available on the prevalence, grading and treatment of truncal acne vulgaris on the chest and back. A study was designed to examine the prevalence and severity of acne on the face, chest, and back in a referral cohort of patients with acne using a validated global acne severity scale. In 965 patients, the prevalence of acne on the face, chest, and back was 92%, 45%, and 61%, respectively. Acne severity was observed to have a much higher correlation between chest and back than face and back or face and chest.

In the largest study to date, it was observed a 35.6% prevalence of acne lesions on both face and trunk among 2,926 patients with mild-to-moderate acne. This group also found that the frequency of truncal acne was significantly higher in patients who had a family history of acne.

Summary of treatment benefits

Retinoids are recognized as having a unique mode of action by reducing formation of acne precursor lesions and limiting development of new lesions.

Because of their preventive action in acne by targeting microcomedones, retinoids should form the cornerstone of therapy.

Unknowns relative to treatment benefits

Risk-benefit impact:
No arguments to consider that a long-term treatment would impact the benefit/risk of the drug.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Aklief, together with measures to minimise such risks and the proposed studies for learning more about Aklief's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

• Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

• Important advice on the medicine's packaging;

• The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

• The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Aklief is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Aklief are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Aklief. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Summary of safety concerns	
Important identified risks	- None
Important potential risks	- Teratogenicity: safety during pregnancy
Missing information	- Use longer than 1 year - Use with concomitant acne medications

II.B Summary of important risks

Important Identified risks: None	
Evidence for linking the risk to the medicine	Not applicable
Risk minimisation measures	Not applicable

Additional pharmacovigilance activities	Not applicable
Important Potential risk: Teratogenicity: safety during pregnancy	
Evidence for linking the risk to the medicine	Studies in animals with trifarotene by the oral route have shown reproductive toxicity at high systemic exposure (see section 5.3). Due to the limited available data and considering the low cutaneous passage of trifarotene, Aklief 50 microgram/g cream should not be used during pregnancy. See SmPC section 5.3 The following information is provided: In animal reproduction studies, oral administration of trifarotene in pregnant rats and rabbits during organogenesis was teratogenic and embryotoxic (…) Non-teratogenic plasma exposures in rats and rabbits were 534 and 98-times higher than the exposure observed in humans, respectively. There are no clinical data on the use of Aklief in pregnancy.
Risk minimisation measures	Routine Pharmacovigilance activities, including use of a targeted follow-up questionnaire for pregnancies. Product labeling in SmPC and PIL: SmPC section 4.3 & 4.6 and PIL section 2. <u>Pregnancy</u> The following recommendations are provided: Aklief is contraindicated during pregnancy or in women planning a pregnancy. If the product is used during pregnancy, or if the patient becomes pregnant while taking this drug, treatment should be discontinued. Information on safety margin for teratogenicity is also provided.
Additional pharmacovigilance activities	None
Missing information: Long term exposure > 1 year	
Risk minimisation measures	Routine risk communication: See SmPC section 4.2. The duration of treatment should be determined by the physician based on the clinical condition. Prescription only medicinal product

Additional pharmacovigilance activities	None
Missing information: Use with concomitant acne medications	
Risk minimisation measures	Routine risk communication: See SmPC section 4.5 There is no data on the pharmacodynamic interaction potential of trifarotene. Caution should be exercised if cosmetics or acne medications with desquamative, irritant or drying effects are concomitantly used with the medicinal product, as they may produce additive irritant effects (see SmPC section 4.4). Prescription only medicinal product
Additional pharmacovigilance activities	None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Aklief.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Aklief.