European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON DOSSIER REQUIREMENTS FOR ONCOLOGY PRODUCTS

AGREED BY EWP	16 March 2005
CONSULTATION OF SWP AND ERAWP BY	6 June 2005
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	15 June 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	30 September 2005

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1. INTRODUCTION

Chemotherapy against cancer diseases has been used for approximately 50 years in human and tentatively also in veterinary medicine. In recent years the knowledge about veterinary cancer therapy has increased considerably and today veterinary oncology is an established area of expertise. There are yet no approved veterinary anti-cancer products available in the European Union and the substances used in non-food producing animals are human medicinal products prescribed according to Directive 2001/82/EEC as amended by Art. 10 No.1 b)i Directive 2004/28/EC (the so called cascade principle). Thus, to encourage such applications, specific guideance to clarify the requirements for cancer product registrations in veterinary medicine is warranted.

2. PROBLEM STATEMENT

Although some requirements for anti-cancer products would be similar to other medicinal products, i.e. existing general guidance is relevant, there are several specific considerations to be made. Classical standards in demonstrating efficacy and target animal safety cannot be used. Anti-cancer compounds are generally more toxic both for animal patients and humans than other drugs on the market today. Classical standards in demonstrating efficacy and target animal safety cannot be used. In addition, the risk for hazardous exposure e.g. to members of the animal's household and the environment resulting from the toxic potential has to be considered.

3. DISCUSSION

The knowledge about cancer therapy in animals is based on experience of the use of medicinal products developed for humans. This experience should be considered when applying for marketing authorisation for anti-cancer products for veterinary use. However, due to the properties of this group of compounds special precautions are needed and existing guidelines do not cover all important aspects relevant for the risk/benefit analysis for anti-cancer medicines. The main topics to be addressed are as follows:

Efficacy

- Consideration should be given to the fact that antineoplastic chemotherapy in animals is palliative.
- Special requirements for dose finding studies dependent on whether toxicity or any pharmacological effect is regarded as dose limiting. Consideration of maximum tolerated dose and individual dose adjustment.
- Special concerns regarding drug interactions and the use of approved medicinal products in multi-drug protocols.
- Specific efficacy criteria for cancer diseases in dogs and cats, e.g. tumour regression and quality of life.
- Special considerations regarding the use of positive controls and rescue protocols.
- The mechanisms of development of resistance should be addressed.

Target animal safety

- Recommendations regarding number of animals needed in order to assess tolerance data, considering the narrow safety margin.
- Special aspects for studies on target animal tolerance, e.g. establishment of maximum tolerated dose in diseased animals.

User safety

- Special formulation requirements to be fulfilled to limit the risk for human exposure.
- Special human safety aspects in cases where not only the product itself but also excreta from treated animals could be toxic.

Environmental risk assessment

- Exposure of the environment: specific precautions for the disposal of any unused product, waste material and excreta from treated animals, if necessary.

Miscellaneous

- Cross-checking existing guidelines for possible inconsistencies.

4. RECOMMENDATION

It is proposed that a guidance document is created to provide recommendations for the demonstration of efficacy and safety (target animal safety, user safety and environmental safety) of anti-cancer products for use in non-food producing animals.

5. TIMETABLE

Jun – Sept 2005	Consultation period
Nov 2005	CVMP: Analysis of comments received and decision on further development of guideline
2 Q 2006	First draft guideline to be discussed in WP(s)
2-3 Q 2007	Draft guideline for discussion and adoption to CVMP

6. RESOURCE REQUIREMENTS FOR PREPARATION

Member States to provide input via EWP (efficacy and target animal safety), SWP (user safety) and ERA ad hoc group (environmental risk assessment). Rapporteurs to prepare the draft guideline. Liaision between (rapporteurs of) working parties might require additional drafting group meeting(s).

7. IMPACT ASSESSMENT (Anticipate)

The anticipated benefit both to industry and regulatory authorities is due to clarifications regarding dossier requirements. This is likely to increase the interest for industry in applying for marketing authorisations for veterinary anti-cancer products and would be beneficial to regulators in assessing such dossiers. Clearer guidance would be given to veterinarians in oncology practice.

8. INTERESTED PARTIES

Pharmaceutical industry.
Regulatory authorities.
Federation of Veterinarians in Europe (FVE), especially veterinarians in oncology practice.
Scientific associations, e.g. European College of Veterinary Internal Medicine-Companion animals (ECVIM-CA).