

Sheep vaccinations: latest research and farmer communication

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With ever-increasing pressures on vets and farmers to minimise use of antimicrobials and anthelmintics in livestock production, vaccination, as well as good husbandry and management, is becoming an increasingly important tool in the control of disease on farms.



Rubbing the injection site over the ribs following administration.

Some diseases may have only one commercially available vaccine, but others, such as clostridial disease, are covered by a large number, each varying in the protection it provides. Vaccines may be live, attenuated or killed and this can have significant implications in terms of specific animals and when they can be used.

This article aims to provide an up-to-date overview of the current commercially available vaccines for sheep in the UK, as well as to discuss other vaccines available via the cascade, and those being developed for use in the future.

Farmer communication

In general, when communicating with farmers it is important to maintain a positive outlook and focus initially on areas where the farmer has most concerns. This will show them you understand their needs and are interested in their business. Once a good relationship has been established,

the opportunity exists to address more significant problems on the farm.

Outcomes from CPD this summer, when more than 120 sheep-keen farm vets shared tips for better sheep farmer engagement, indicated the most important factors were showing farmers we were interested in their animals and that we could provide a good value service to reflects this.

Practically, communication with farmers can be done in a number of ways, including timely newsletters, discussion groups or farmer meetings, posters displayed around the practice and text message or email alerts. It is important to determine the methods that work best for your individual clients so channels of communication remain open long term.

Regarding vaccinations, it is important to first consider whether the vaccines we are recommending or are currently used on farm are appropriate and being utilised to best effect. While some vaccines can only be sourced on prescription, a number are available through livestock merchants without a prescription. It is essential we, as vets, ensure all vaccines are used in the appropriate situation and are stored and administered according to manufacturers' instructions. The key to this is a good vet/farmer relationship. Vets must have a good working knowledge of each farm under their care to ensure farmers are getting the most from their vaccines.

It may be the only contact a veterinary practice has with some flocks is when those managing them come in once a year to purchase a vaccine. This can provide a great opportunity to start a conversation about disease control strategies and any new or persistent problems in the flock. Discussing the use of a vaccine can open up to a more general discussion on potential changes to management and biosecurity that may be a relatively low-cost, but highly effective, way of aiding disease control.

Management of sheep has a major impact on disease control and, therefore, the perceived success of any vaccination protocol. Identifying husbandry factors that limit the success of vaccines is, therefore, essential (Paton, 2013). The strength of immunity induced by any vaccine will depend on the condition the target animal was in at the time of vaccination.

Poor nutritional status, as well as concurrent disease, will have a negative effect on response to vaccination. Equally significant is the way a vaccine is stored and administered, as well as the level of disease burden within the environment or sheep population. It is vital farmers understand these limitations before starting a vaccination programme.

Vaccinations should be targeted at diseases likely to provide the most benefits, either economically or through improved welfare – and ideally both. It is essential any newly proposed vaccination protocols are properly costed out against the cost of disease. It is important to prove the use of a vaccine is cost effective, as well as good for animal health and welfare.

Decisions on vaccine usage should be taken only after consideration of all the factors to have an

impact on the flock, including the availability of labour to administer the vaccine (Paton, 2013).

Abortion vaccines

Currently four abortion vaccines are commercially available in the UK. Enzovax (MSD Animal Health) and Cevac Chlamydia (Ceva) are live vaccines for protection against enzootic abortion in ewes (EAE). Mydiavac (Benchmark Animal Health) is an inactivated vaccine against EAE and can be used in the prevention of enzootic abortion infection, as well as in the face of an outbreak to reduce the number of abortions. Finally, Toxovax (MSD Animal Health) is a live vaccine for protection against the losses caused by toxoplasmosis.

At the same time, with surveys suggesting a large majority of flocks are exposed to *Toxoplasma gondii*, there is an argument to suggest all breeding ewes should be vaccinated before first going to the ram.

When considering whether to use an abortion vaccine in a sheep flock, it is necessary to carry out a full disease risk assessment and consider the flock's current status. Serology is useful in this regard. It is only then that the most appropriate disease control measures can be determined.

It is important to note EAE infection usually occurs in the lambing season before symptoms are seen and, therefore, some ewes are likely to be already incubating disease before a vaccination protocol is started. As a result, despite vaccination, some (incubating) ewes will still abort, but it is likely the incidence of abortion in these incubating ewes will be lower in vaccinated flocks. Live EAE vaccines should not be administered to animals being treated with antibiotics, particularly tetracyclines.

There is no test to detect EAE in carrier animals prior to the abortive event, by which time they are likely to have already infected other individuals. It is, therefore, not possible to eradicate this disease from an already infected flock and indicates the importance of initiating vaccination before introduction of disease. However, following administration of a live vaccination in a flock, no way is available to distinguish between infected and vaccinated animals, so EAE accreditation becomes unattainable. This may be an important consideration for some flocks.

A three-year investigation, between 2011 and 2013, used molecular tools to consider abortions from sheep that had been previously vaccinated with a commercial, live, attenuated *Chlamydophila abortus* vaccine. Vaccinal strains were found in approximately 30% of all *C abortus* samples, with the remaining samples wild type. Further investigation is required, but the live vaccines have been used successfully for many years to reduce abortion losses and, therefore, their use in the control and prevention of EAE would still be advocated (Livingstone et al, 2014).

With the use of toxoplasmosis vaccine, it is worth remembering that often the older animals in the flock will have previously been exposed and will consequently show historical titres on serology.

This can be an important consideration in the decision of how many of the flock should be vaccinated following detection of disease for the first time. It may be it is only necessary to vaccinate the younger cohorts of ewes, with considerable cost-saving to the client.

No vaccines are available in the UK to protect against *Campylobacter* abortion, the third most common cause of abortion in the UK. Campyvax 4 (MSD Animal Health) is commonly used in New Zealand to protect against abortions and perinatal losses due to *Campylobacter fetus* subspecies *fetus* and to elicit a specific immune response against *Campylobacter jejuni*. This is a killed vaccine requiring two doses four to eight weeks apart, pre-tupping, followed by an annual booster. It can be imported from Australia, where it is manufactured, under special import licence from the VMD.

A *Campylobacter* abortion storm can have a considerable impact on flocks and although good natural immunity within the flock often remains for the subsequent couple of years, outbreaks can occur – often on a three-yearly cycle. Despite strain variations between UK and New Zealand *Campylobacter*, this vaccine is successfully and economically used on a number of UK farms.

Multivalent clostridial and *Pasteurella* vaccines

Clostridial vaccination is a bit of a minefield, as a large number of vaccines are available, each one protecting against different combinations of diseases. It is important to guide the farmer into making the correct choice for his farm, while understanding the limitations of his or her decision. Carrying out a risk assessment can be the best way forward here.

Essentially, breeding ewes should be covered with a seven, eight, or 10-in-one vaccine to ensure protection of themselves, as well as their young lambs, from diseases such as lamb dysentery. Lambivac (MSD Animal Health) may be useful in situations where maternally derived immunity is important, but a desire exists to limit components within the vaccine to reduce challenge to the immune system (useful, for example, in breeding goats). There is no need for males and non-breeding females to carry antibodies to neonatal diseases, hence the four-in-one Ovivac P Plus (MSD Animal Health) suffices.

It is the authors' experience farmers regularly fail to realise clostridial organisms are ubiquitous in soil and that no farm is free from potential risk. Best practice suggests the whole breeding flock should be covered and, of course, this includes rams.

The authors estimate that even on farms that consider themselves to be “on the system”, a large number of farmers fail to vaccinate their rams or fail to ensure replacement ewes are correctly given the primary course followed by a booster within 12 months. It is certainly not safe to assume correct protocols are in place.

While the protection against clostridial diseases afforded by these multivalent vaccines will generally last one year, the protection against the *Pasteurella* component will not. Protection

against *Pasteurella* will last only a few months after the initial doses and, therefore, in flocks with significant *Pasteurella* problems, a repeat dose may be necessary prior to any anticipated risk period.

Table 1. Comparison of multivalent Clostridial (+/- *Pasteurella*) vaccines available in the UK

	Coveshin 10	Coveshin 8	Biracatin 10	Heptavac P Plus	Ovivoac P Plus	Lambivac	Ovipast Plus
<i>Clostridium perfringens</i> type A	•		•				
<i>Clostridium perfringens</i> type B	•	•	•	•		•	
<i>Clostridium perfringens</i> type C	•	•	•	•		•	
<i>Clostridium perfringens</i> type D	•	•	•	•	•	•	
<i>Clostridium chauvoei</i>	•	•	•	•	•		
<i>Clostridium novyi</i> type B	•	•	•	•			
<i>Clostridium septicum</i>	•	•	•	•	•		
<i>Clostridium sordellii</i>	•		•				
<i>Clostridium tetani</i>	•	•	•	•	•	•	
<i>Pasteurella haemolytica</i>				•	•		•
<i>Pasteurella trehalosi</i>				•	•		•

Ultravac (Zoetis), a vaccine used for the immunisation of sheep (and cattle) against *Clostridium botulinum* types C and D, is not currently available in the UK, but can be obtained under special import licence from Australia.

Table 1. Comparison of multivalent Clostridial (+/- *Pasteurella*) vaccines available in the UK.

Where ewes are vaccinated prior to lambing to confer immunity in lambs via passive transfer, it should be remembered colostral antibodies to the *Pasteurella* component will last only two to four weeks in comparison to 12 to 16 weeks for clostridial antibodies. **Table 1** compares vaccines currently available in the UK.

Footrot vaccine

Footvax (MSD Animal Health) is used for the active immunisation of sheep against *Dichelobacter nodosus*, to aid in the prevention and treatment of foot rot. Vaccination is one of the key elements of the industry-accepted five-point lameness plan for reducing lameness due to foot rot.

It is essential the correct diagnosis is made prior to introduction of this vaccine. Although Footvax contains all UK strains of *Dichelobacter* but no treponemes, its use has been shown to reduce levels of both footrot and contagious ovine digital dermatitis (CODD) on farm (Duncan et al, 2012). This is not surprising as a distinct synergy can be seen between the agents causing footrot and CODD, with each disease exacerbating the other.

Vaccination protocols vary depending on the severity of the disease present, environmental conditions and individual flock circumstances, and must be tailored to suit an individual flock. This goes back to having a good working relationship with the farmer and knowledge of the farm. If this

vaccine is given as a preventive, this should be carried out approximately one month prior to the anticipated risk period and initially two doses should be given as a primary course.

This vaccine can be used immediately in the face of an outbreak to reduce the spread and severity of disease, although it is not advised as an alternative to the rapid treatment of clinical cases with an effective antibiotic and isolation of affected sheep from the rest of the group.

Computer modelling work, which attempts to consider all costs of lameness, including loss of production, suggests a cost benefit to vaccination with Footvax when the levels of lameness due to footrot exceeds 2% of the farm's ewes at any one time (Lovatt, 2015).

Vaccination site reactions are not uncommon and appear to be worse if the vaccine is not warmed to room temperature after removal from the fridge. As a result, this vaccination should not be administered within six to eight weeks of shearing, and warnings should be given to owners of show sheep.

The authors advise farmers to undertake vaccination with Footvax with extreme care, taking time to carefully vaccinate clean, dry sheep subcutaneously. A few cases of late have involved thin ewes being inadvertently given Footvax into their cervical spine, causing unexpected neurological signs in the fortnight following vaccination.

This vaccine is not licensed to be given alongside any other vaccine and it is essential sheep that have previously been given Footvax are never injected with 1% moxidectin (this does not apply to 2% or oral moxidectin). Moxidectin 1% contains Tween or Polysorbate-80, a non-ionic surfactant in an aqueous solution thought to cause hypersensitivity following reaction with the mineral oil base of the Footvax. It is worth bearing in mind Tween is commonly used in vaccines as an emulsifier as it allows for a uniform suspension, and it is a component of both Gudair and Porcilis Ery.

Although we are not aware of published reports, the possibility remains of adverse reactions following the use of these products in sheep previously given Footvax.

Louping ill vaccine

Louping Ill Vaccine (MSD Animal Health) is used for the active immunisation of sheep to stimulate a serological response to the louping ill virus. This is of relevance to the minority of flocks kept in tick areas where it is known the ticks are infected with this flavivirus.

The onset of immunity is four weeks and, therefore, the vaccine should be administered at least four weeks prior to the anticipated risk period. Generally, it is only necessary to vaccinate hogs or newly introduced ewes, prior to the spring rise of ticks. This is another vaccine where injection site reactions are not uncommon, due to the oil-based adjuvant.

Bluetongue vaccines

At the time of writing, both Zulvac 8 Ovis (Zoetis) and Bluevac BTV8 (CZV; distributed via MSD) were expected to become available in mid-July 2016, for the prevention of viraemia caused by bluetongue virus serotype 8 (BTV-8) in sheep and to ensure no onward spread of the disease by the *Culicoides* midge.

Both vaccines require two doses, given three weeks apart, with immunity established three weeks after the second dose and lasting for 12 months. Both vaccines report a small transient increase in rectal temperature in a small number of animals in the day immediately following vaccination.

The Joint campaign Against Bluetongue (JAB) has put together all of the relevant information to help vets to advise farmers in how best to protect their stock against the risk of a bluetongue outbreak, predicted to reach mainland UK by late summer (BVA, 2016).

Schmallenberg vaccines

A number of different Schmallenberg vaccines have been available in that past few years, but to the knowledge of the authors, none are currently available.

Orf/contagious pustular dermatitis vaccines



Handling of pregnant ewes should be as calm and stress free as possible.

Scabivax Forte (MSD Animal Health), the only commercially available vaccine in the UK against contagious pustular dermatitis (orf), is a good example of where the timing of a vaccination can be crucial. This is a live scarification vaccine and, as such, will produce a skin lesion similar to that of the disease itself in the area of the body it is applied to.

It is essential, therefore, that if ewes are to be vaccinated prior to lambing they are not moved to their lambing accommodation (be that pastures or indoor housing) until all lesion scabs have fallen off – at least seven weeks following vaccination.

It is also important vaccinated animals do not have contact with unvaccinated animals during this period, and that they are not shorn or slaughtered. Equally, this is not a vaccine that should be employed unless there is a significant problem with orf on the farm already. Lambs can be vaccinated from one day old if necessary, but it is advisable to wait until they are turned out to reduce the risk of significant environmental contamination.

Johne's disease vaccine

Gudair (manufactured by Zoetis Australia, but marketed in the UK by Virbac) is an inactivated vaccine for the active immunisation of sheep and goats to stimulate cell-mediated and humoral immunity against *Mycobacterium avium* subspecies *paratuberculosis* infection, as an aid in the control of Johne's disease.

The vaccine offers protection against the development of clinical ovine Johne's disease (OJD), reduces mortalities associated with OJD, gradually decreases the prevalence of flock infection and decreases faecal shedding of *M avium paratuberculosis*. A single vaccine dose provides lifelong immunity.

Vaccination of breeding sheep should be undertaken when they are younger than a year old. Most recommendations were for the vaccine to be given in the first few days of life, although some reports have seen more benefit in older sheep for reasons of management, grouping and immune maturity. Introduced sheep should be vaccinated on arrival into an infected flock and kept isolated for a month.

Caseous lymphadenitis vaccine

Glanvac 3 (Zoetis), a multivalent clostridial vaccine that includes caseous lymphadenitis (CLA) components, is not currently available in the UK, but can be obtained under special import licence from Australia. The VMD reports approximately 25,000 doses are officially imported annually into the UK, although some indications from the industry suggest the total volume of imports may actually be double this.

UK farmers report good field control following use of the imported Australian vaccine, despite phenotypic differences in the clinical presentation of CLA infections in Australia and the UK. It has been suggested that without further efficacy data, the existing Australian vaccines may not be wholly protective or appropriate for use in the UK (Sheep Veterinary Society; SVS), and even in Australia the vaccine only produces a reduction in the prevalence and severity of disease in a flock.

Concerns have also been raised about the possibility of inducing a carrier status in vaccinated animals. Currently, vaccination can interfere with serological testing of sheep in the UK (SVS, 2000). Research at Moredun has shown all strains of *Corynebacterium pseudotuberculosis* across the world are highly related, suggesting common control measures may be effective (Fontaine, 2015). A UK-produced differentiating infected from vaccinated animals (DIVA) CLA vaccine has been discussed for some years, although this has not yet become commercially available. Informal industry discussions have indicated that while parts of the pedigree industry are keen for a DIVA vaccine, its uptake would only be significant at the right price, due to the current widespread use of the competitively priced Australian vaccine.

***Staphylococcus aureus* vaccine**

VIMCO (HIPRA, Portugal) is not currently available in the UK, but can be imported under special licence from Portugal. This vaccine can be used to reduce the incidence of subclinical mastitis (reduction in udder lesions, somatic cell count and *Staphylococcus aureus* count) due to *S aureus*.

It must be administered to the entire flock five weeks before the expected date of lambing, with a second dose three weeks later. Annual boosters prior to lactation are required. It is important to note vaccination is only one component of a complete mastitis control plan.

Anecdotal evidence from a few farms using the vaccine suggests it may help to reduce the incidence and severity of mastitis cases. It may, therefore, be helpful in certain flocks with a high incidence of mastitis as an adjunct to other control strategies.

Erysipelas polyarthrititis vaccine

Eryvac (Zoetis) can be obtained under special import licence from Australia as it is not currently available in the UK. It is used for the control of erysipelas lameness in lambs through vaccination of ewes pre-lambing, conferring passive immunity to the lambs, via colostrum, for the first six to eight weeks of life.

Some reports are available of the successful off-licence use of Porcilis Ery (MSD Animal Health) in flocks with erysipelas polyarthrititis. While the product is a POM-VPS, its use in sheep, under the cascade, must be prescribed by a veterinary surgeon who has the animals under his or her care. Two doses of vaccine, four weeks apart, have been suggested by some sources, as an initial course followed by an annual booster four to six weeks pre-lambing.

Although anecdotal reports indicate use of this vaccine may have reduced the incidence of joint ill in young lambs, no robust studies based on diagnostic evidence have been carried out, and reports suggest the vast majority of joint ill is caused by *Streptococcus dysgalactiae*. The authors have been made aware of some adverse reactions (deaths and abortions) following the use of Porcilis Ery in pregnant ewes.

Bovine viral diarrhoea vaccine

Previous work by Moredun has shown no cross protection against Border disease virus (BDV) in sheep when a bovine viral diarrhoea (BVD) vaccine is used (Brun, 1993). However, some reports from France indicate BVD vaccine being used in sheep at half or one-quarter of the cattle dose, while a small-scale study by Meyer et al (2010) demonstrated the presence of neutralising antibodies to both old and new strains of BDV following vaccination with half-dose Bovilis BVD (MSD Animal Health).

Further studies are ongoing to assess the efficacy of sheep vaccination against a BDV challenge.

***Haemonchus contortus* vaccine**



Plenty of good handling facilities are on the market.

Barbervax has been developed to aid in the reduction of *Haemonchus contortus* egg shedding. It is effective against all *H contortus* worms, including any anthelmintic resistant ones. This vaccine was developed through collaboration between Moredun and PathWest Albany Laboratory in Western Australia, where it is manufactured.

This vaccine has been extensively trialled in Merino sheep and commercially available and in high demand in Australia since 2014. The vaccine is currently not available in the UK, but is now going through the licensing process in South Africa.

The vaccine contains tiny amounts of protein, purified from the lining of the *H contortus*' intestines. The antibodies produced by vaccinated sheep circulate in the sheep's blood and are taken up by the worm when feeding. The antibodies attach to the lining of the worm's gut, blocking digestion, effectively starving the worm and resulting in the production of fewer worm eggs and eventual worm death.

This vaccine is given to lambs as a series of five subcutaneous injections, with the first three given at three-to-four-week intervals and then subsequent injections at six-week intervals to cover the *H contortus* risk period.

This protocol must be strictly adhered so satisfactory protection is achieved. This vaccine can be administered at the same time as other vaccines and anthelmintics and is safe to use in young lambs and pregnant ewes. It is essential to note this vaccine provides no protection against other gastrointestinal nematodes, so regular faecal egg count monitoring should still be carried out on vaccinated lambs.

Grazing management, to make the most of lower-risk grazing, will further enhance the effectiveness of this vaccine, while breeding for worm resistance and resilience will help with more long-term worm control.

The future

Looking ahead, parasite vaccines may be developed to treat the following conditions:

Liver fluke

Fasciola hepatica is one of the most important trematodes affecting global ruminant production and a considerable amount of research has been carried out examining the way the parasite can down-regulate aspects of the host immune response, to ensure its survival within the host. It may be possible to use the multiple immunomodulatory molecules released by *F hepatica* as components of a vaccine to induce a circulating antibody (protective) response. The difficulties with this lie in trying to raise an antibody to an active immunosuppressive molecule, so the specific activity of the antigen may need to be inactivated prior to use as a vaccine (McNeily and Nisbet, 2014).

Teladorsagia circumcincta

Moredun has had a major focus on *Teladorsagia circumcincta* in the past 10 years and in 2013 it published a paper describing a recombinant vaccine cocktail to control *T circumcincta* (Nisbet et al, 2013). This was the most effective recombinant vaccine yet described to control a parasitic nematode of ruminants in the definitive host. Since 2013, the vaccine has been refined, aiming to reduce the number of antigens included as well as addressing variability in efficacy in young lambs and measuring efficacy in pregnant and lactating ewes. Progress continues, but this vaccine is not

yet at a commercial stage.

Sheep scab

Work by Burgess et al (2016) at Moredun has resulted in the development and validation, in repeated immunisation and challenge trials, of a seven recombinant protein (*Psoroptes ovis* antigens) sub-unit cocktail vaccine for sheep scab. Vaccination resulted in significant reductions in lesion size (63% reduction) and mite numbers (56% reduction) following challenge.

The group aims to further develop the vaccine in the next few years, increasing efficacy and refining the cocktail of antigens to make it more commercially feasible to produce. However, it is unlikely final efficacy will exceed 90%, so vaccination should not be considered as a single control measure, but as one of many tools for coordinated control of a sheep scab outbreak. The current diagnostic test is unable to distinguish between vaccinated and infested animals, but additional antigens can be incorporated within the test to enable this in the future (Burgess et al, 2016).

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