

An update on treatment of FIP in the UK

Dr. Sam Taylor BVetMed(Hons) CertSAM DipECVIM-CA MANZCVS FRCVS

Prof. Séverine Tasker BVSc BSc DSAM PhD DipECVIM-CA FHEA FRCVS

Prof. Danielle Gunn-Moore BSc(Hon), BVM&S, PhD, MANZCVS, FHEA, FRSB, FRCVS

Dr. Emi Barker BSc BVSc PhD PGCertTLHE DipECVIM-CA MRCVS

Dr. Stephanie Sorrell BVetMed(Hons) MANZCVS DipECVIM-CA MRCVS

The above specialists have come together to run the 'FIP advice' email address (fipadvice@gmail.com) answering queries on the new treatments on a voluntary basis and disseminating information to vets and vet nurses in the UK. So far, they have answered over 100 emails on the advice line

Introduction

In August 2021 remdesivir (Figure 1) became legally available to UK vets for the treatment of FIP in cats. Since that time many cats and kittens have been treated and are still being treated successfully. As with any novel formulation, with experience, adjustments are made in protocols and given the recent release (November 2021) of oral GS-441524 (50mg tablets) from a specials manufacturer in the UK (Figure 2), this article has been created to support practitioners in the use of remdesivir and GS-441524 in the management of FIP. It is worth remembering that treatment may need to be tailored to the individual cat based on response, compliance and client finances. Specific protocols are listed below to help vets make decisions with their clients, but will not be appropriate for all.

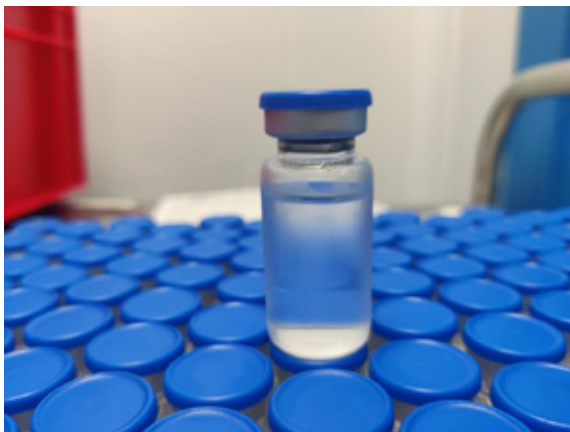


Figure 1: Remdesivir for intravenous or subcutaneous injection

Treatment protocols (updated November 2021)

Drug dosages have increased from previous recommendations, based on the experience of our Australian colleagues who have treated over 600 cats. Although some cats responded to the previously recommended lower dosages, they found that recurrence at, or towards the end of, the 84-day (12-week) treatment period was possible, resulting in the need for extension of the treatment at a higher

daily dosage. This was ultimately more expensive than if the treatment course had been started at a higher dosage.



Figure 2: Oral GS-441524 tablets

When using remdesivir and/or GS-441524, treatment options now include a 12-week course of injectable remdesivir, transition from injectable remdesivir to oral GS-441524, or an entirely oral GS-441524 protocol. Suggested dosages, benefits and limitations of each protocol are provided below. Remdesivir cannot be given orally. Recommended drug dosages (Table 1) depend upon clinical presentation – i.e. whether there is an effusion present or not and whether there is ocular and/or neurological involvement – this is due to variation in the tissue penetration of the drugs. Where there is doubt, use of the higher dosage is preferable.

Please note that these dosages of oral GS-441524 are higher than quoted in some publications – this is because these publications have used 'black market' preparations of so-called GS-441524 in which the amount of active agent given to the cats was not confirmed. The dosages provided in this article are based on experience using an oral preparation of

Need advice on the treatment of FIP?

If advice is needed on the diagnosis and treatment of a suspected case of FIP, please email fipadvice@gmail.com

known GS-441524 content legally available in the UK and Australia. Thus extrapolation is not applicable to other oral preparations where the active component and/or its concentration are not known or given by the manufacturer.

Combined injectable & oral treatment protocols:

The decision on when to move from injectable remdesivir to oral GS-441524 may depend on the cat's tolerance of injections (or oral administration of tablets), formulation price differences (including cost of needles, syringes, sharps disposal, wastage), owner preferences and finances.

Experience suggests this transition can be made between 7 and 14 days of starting remdesivir IV or subcutaneous treatment. The change can be made directly; remdesivir is given one day and GS tablets

started the next day.

The protocol chosen will depend on the severity of the FIP disease in the cat. Dosages are shown in Table 1.

Severe disease (anorexic, dehydrated, cat usually will be hospitalised)

1. Initial treatment with once daily intravenous remdesivir (Table 1) for 3-4 days i.e. on days 1, 2, 3 ± 4. This provides a loading dose of the drug. On each day, dilute the remdesivir dose required to a total volume of 10ml with saline and administer slowly over 20-30 minutes manually or with a syringe driver.
2. Follow with once daily subcutaneous remdesivir at the same dosage (Table 1) up to day 7-14
3. Change to once (or twice) daily oral GS-441524 (Table 1) on day 8-15, and continue until at least day 84.

Table 1: Summary of dosage recommendations for remdesivir and GS-441524

Clinical presentation	Remdesivir – by injection	GS-441524 – oral
Cats with effusions and without ocular or neurological signs	10 mg/kg once daily	10-12 mg/kg once daily
No effusion and without ocular or neurological signs	12 mg/kg once daily	10-12 mg/kg once daily
Ocular signs present (effusive and non-effusive)	15 mg/kg once daily	15 mg/kg once daily
Neurological signs present (effusive and non-effusive)	20 mg/kg once daily	10 mg/kg twice daily (i.e. 20 mg/kg given as a divided dose)

Less severe disease (normal hydration, eating)

1. Initial treatment with once daily subcutaneous remdesivir (Table 1) up to day 7-14
2. Change to once (or twice if very high neurological dosage needed) daily oral GS-441524 (Table 1) on day 8-15, and continue until at least day 84.

Oral only treatment protocol:

An oral GS-441524 treatment only protocol is recommended if injectable not tolerated/ possible financially:

1. Once (or twice if very high neurological dosage needed) daily oral GS-441524 (Table 1) until at least day 84.

Potential adverse effects of remdesivir

Remdesivir seems well tolerated. However, the following adverse effects have been reported:

- Transient local discomfort/stinging on injection (see later on prevention);
- Development/worsening of a pleural effusion (not always proteinaceous) in the first 48 hours of treatment, sometimes requiring drainage;
- Cats may seem depressed or nauseated for a few hours after IV administration;
- Increases in ALT enzyme activity have been reported (unclear if due to underlying FIP disease or an adverse drug effect);
- Mild peripheral eosinophilia has been reported.

NOTE ON WEIGHING CATS: It is very important to weigh cats weekly during treatment, using accurate scales – weight gain and/or growth in kittens will occur with successful treatment necessitating an increase in dose to ensure that the dosage of antiviral administered is still appropriate for the type of FIP being treated.

Options for cost limited clients – please note that, ideally, therapy should be given using the recommended formulations and dosages for as long as possible (up to 84 days) to increase likelihood of cure. Only take the options below if absolutely necessary, as relapse may occur, which then requires longer treatment, increasing costs;

Need advice on the treatment of FIP?

If advice is needed on the diagnosis and treatment of a suspected case of FIP, please email fipadvice@gmail.com

- Give oral GS-441524 treatment only for 84 days, as outlined above;
- Give injectable remdesivir or oral GS-441524 for as many days as the owner can afford before switching to oral mefloquine 62.5mg 2-3 times weekly (large cat, give 3 times a week) or 20-25mg orally once daily (if reformulation of tablets is possible e.g. PCCA Ltd) for completion of an 84-day treatment protocol; mefloquine is cheaper than remdesivir and GS-441524 but more research is needed to judge its effectiveness in this situation;
- If an increase in remdesivir dosage is required (e.g. due to neurological disease appearing during treatment) but cannot be afforded, mefloquine treatment can be added as adjunct treatment, as this is cheaper than remdesivir, although more research is needed to judge the effect of this combination;
- Feline interferon omega has also been used in the

period following treatment with remdesivir/GS-441524 treatment, but further research is needed on this combination to judge if it is necessary.

Are oral treatments given with or without food?

- GS-441524 is given on an empty stomach (wash down with a little water) – food can be given 30 mins after treatment;
- Mefloquine is given with food, otherwise vomiting often results.

Do not forget to support clients giving oral medications, as this can also be challenging. Direct clients to the iCatCare website for information and videos:

<https://icatcare.org/advice/how-to-give-your-cat-a-tablet/>

What can I do to help the owners give the subcutaneous remdesivir?

Injection with remdesivir can cause transient local discomfort. The following may help reduce discomfort and improve compliance:

- Ensure owners use a new needle each time to withdraw the drug from the bottle (this will reduce the risk of bacterial contamination of the bottle, as well as alcohol swabbing the reusable seal top of the bottle before entry of the needle);
- Ensure owners change the needle after withdrawing the drug from the bottle and before injection (puncturing the reusable seal will blunt the needle);
- Needle size preference varies; some prefer a 21G needle to make injecting quicker, others find a finer 23G needle is better tolerated, so it may be worth trying both if problems arise;
- Rotate the injection sites;
- Have remdesivir at room temperature before administration;
- Oral gabapentin (50 to 100 mg per cat) may be helpful and/or transmucosal or subcutaneous buprenorphine given at least 30-60 mins before the remdesivir injection to induce mild sedation/analgesia;
- The area to be injected can also be clipped to help owners locate the appropriate site to inject and so that topical EMLA cream can be applied 40 mins before injection, although surface desensitisation may not help as it is usually the remdesivir under the skin that causes discomfort;
- Ensure the full dose of injection is administered at each time-point and encourage owners to report any mishaps as this may influence decisions if relapse occurs;
- Cats will need several weeks of treatment. Encourage owners to make the injection experience more positive by using treats (e.g. Lick-e-lix, Dreamies) around the time of injection, or stroking, brushing, or playing with the cat if they are less food motivated. Suggest owners spend time each day with their cat positively engaged to avoid any damage to cat-owner relationships that can reduce compliance.

What should I expect during treatment?

- In the first 2-5 days you should see an improvement in demeanour, appetite, resolution of pyrexia and reduction in abdominal (Figure 3) or pleural fluid if an effusion is present (note that in some cases pleural fluid can transiently worsen in the first couple of days– if the cat is at home, advise owner to measure resting respiratory rate, plus respiratory effort) – effusion typically resolves by 2 weeks;
- If an effusion is still present at 2 weeks, consider increasing dosage to one that is greater than that

being used e.g increasing the dosage from that used for cats with effusions only;

- Serum albumin increases and globulin decreases (i.e. they normalise) over 1-3 weeks, but note that globulins can initially increase when a large volume effusion is absorbed;
- Lymphopenia and anaemia may take longer to resolve, up to 10 weeks;
- Mild peripheral eosinophilia is a common finding and may be a favourable marker for disease resolution, as it is in COVID patients;

Need advice on the treatment of FIP?

If advice is needed on the diagnosis and treatment of a suspected case of FIP, please email fipadvice@gmail.com

- Lymph node size reduces over a few weeks;
- If progress is not as expected, consider reviewing the diagnosis (see below) and/or increasing dosage.



Figure 3: A cat with FIP and ascites. Effusions should start to resolve over 3-5 days after starting treatment

What do I need to monitor during treatment?

- Ideally, serum biochemistry and haematology after 2 weeks and then monthly;
- For cost limited clients, monitor weight/demeanour/effusions (e.g. by in-house scanning)/neurological signs/key biochemical abnormalities only (e.g. measuring just globulin, bilirubin or spinning microhaematocrit tube for PCV/TP/colour of plasma);
- NB. ALT enzyme activity may increase – it is not clear if this is due to FIP pathology vs. drug reaction, and it is not usually a reason to stop therapy. It is not known if the addition of hepatoprotective therapy (e.g. SAME) is helpful in these cases;
- Point-of-care ultrasonography (POCUS) to monitor for effusion resolution and/or lymph node size.

If I am seeing a positive response to treatment, when do I stop treatment?

- Not before 84 days (12 weeks);

- Confirm resolution of previous abnormalities (clinically, POCUS, serum biochemistry, and haematology);
- Only stop treatment once cat has been normal (clinically and on serum biochemistry and haematology) for at least 2 weeks (ideally 4 weeks).

If I am seeing no response or only a partial response to treatment, what do I do?

- Ensure that you are still confident that the cat has FIP – review diagnosis, look for additional pathology, consider repeat sampling (e.g. external laboratory analysis of any fluid; cytology or biopsy of lymph nodes);
- If biochemical abnormalities (hyperglobulinaemia and the albumin to globulin ratio in particular) remain present after 6-8 weeks, then increase dose as for relapse (below) by 3-5 mg/kg per day and continue the course, not stopping until parameters normalise for at least 2 weeks as stated above for ‘when do I stop treatment?’ – This may well include extending the course over 12 weeks.

What do I monitor after treatment?

- Advise the owner to monitor the cat closely for any clinical relapse – this monitoring should continue for 12 weeks after completion of treatment;
- Ideally, repeat serum biochemistry and haematology two weeks and one month after stopping treatment (to detect any changes that could suggest early relapse);
- Note that relapse can occur with clinical signs but without any significant biochemical/haematological abnormalities.

In the event of relapse

e.g. recurrence of effusion, pyrexia, development of ocular or neurological signs, or return of hyperglobulinaemia:

- Ensure that you are still confident that the cat has FIP – review diagnosis, look for additional pathology, consider repeat sampling (e.g. external laboratory analysis of any fluid; cytology or biopsy of lymph nodes);
- If relapse occurs after completion of treatment – restart treatment with remdesivir or GS-441524 at a higher dosage (typically 3-5 mg/kg higher per day than dosage used previously) and treat for another 12 weeks. The increased dosage used depends on the dosage the cat is on at the time of the relapse and the

Neutering & routine treatments during therapy for FIP

- Neutering is ideally performed a month after treatment is completed if the cat has responded. However, if leaving unneutered is causing much stress e.g. attempts to escape or distress when queens are on heat, neutering during the treatment course may be preferred. If the latter is needed, neutering should ideally be performed at a time when the cat is doing well on treatment and still has 2 weeks of treatment remaining following the date of neutering (so antiviral treatment ongoing at a potential time of ‘stress’ after neutering);
- There is no contraindication to routine worming and flea treatment for cats on remdesivir or GS-441524;
- No information is available on vaccination of cats receiving treatment for FIP. Vaccines should be administered as normal if the cat is well during treatment, as still likely to be protective. For cats that have received an initial course, consider providing a third dose of vaccine after completion of FIP treatment (see WSAVA Vaccination Guidelines);
- If veterinary procedures are necessary, clinic stays should be minimised, and Cat Friendly Clinic (www.catfriendlyclinic.com) protocols and handling implemented to avoid stress to the cat.

nature (e.g. severity and/or development of neurological signs) of the relapse, but can be up to that recommended for neurological FIP (20 mg/kg - see Table 1 earlier). It is possible some cats will respond to a shorter course but ideally treatment for relapse after completion of a course of treatment is continued for the full 12 weeks to limit repeat relapse;

- If it is not possible to increase the dose of remdesivir or GS-441524 (e.g. the highest neurological dosage of 20 mg/kg is already in use), consider use of mefloquine as adjunct treatment (see above) whilst continuing remdesivir or GS-441524 treatment at the same dosage.

Adjunctive treatments

- If the cat is on prednisolone treatment, this should be stopped whilst giving remdesivir or GS-441524, unless it is required for short term management of specific immune-mediated disease arising as a result of FIP e.g. haemolytic anaemia;
- Supportive therapies such as antiemetics, appetite stimulants, fluid therapy and analgesics can be given with remdesivir or GS-442415 as required.

Potential future updates

We are constantly learning about treatment with

these drugs and advice may change in time. Other agents, e.g. protease inhibitors (e.g. GC374) and other nucleoside analogues (e.g. molpurnavir) have also been trialled in cats, but are not commercially available at this time. How these agents and other immunomodulatory agents (e.g. polyprenyl immunostimulant) will fit into a future protocols is unknown at this time.

Updated 10th March 2022

Thank you to Richard Malik and Sally Coggins for their advice and assistance producing this document.

Dr. Richard Malik DVSc MVetClinStud PhD FASM graduated from the University of Sydney in 1981. He is a specialist in small animal internal medicine and has a special interest in infectious diseases of dogs and cats. He works for the Centre for Veterinary Education helping to organise CPD.

Dr. Sally Coggins BVSc (hons I) MANZCVS (Feline Medicine) graduated with first-class honours from The University of Sydney in 2007. Sally is currently investigating novel antiviral therapeutics for Feline Infectious Peritonitis and is currently conducting clinical trials open for national recruitment.

**Join ISFM Membership
and be at the forefront of
feline veterinary care**

icatcare.org/veterinary/isfm



isfm

International Society of Feline Medicine

ISFM supports the creation of evidence-based documents to support vets with their clinical decision making and encourages the collaboration of experts to help cats. For further information on ISFM's work and becoming a member visit <https://icatcare.org/veterinary/isfm/vet-membership/>.

Need advice on the treatment of FIP?
If advice is needed on the diagnosis and treatment of a suspected case of FIP, please email fipadvice@gmail.com