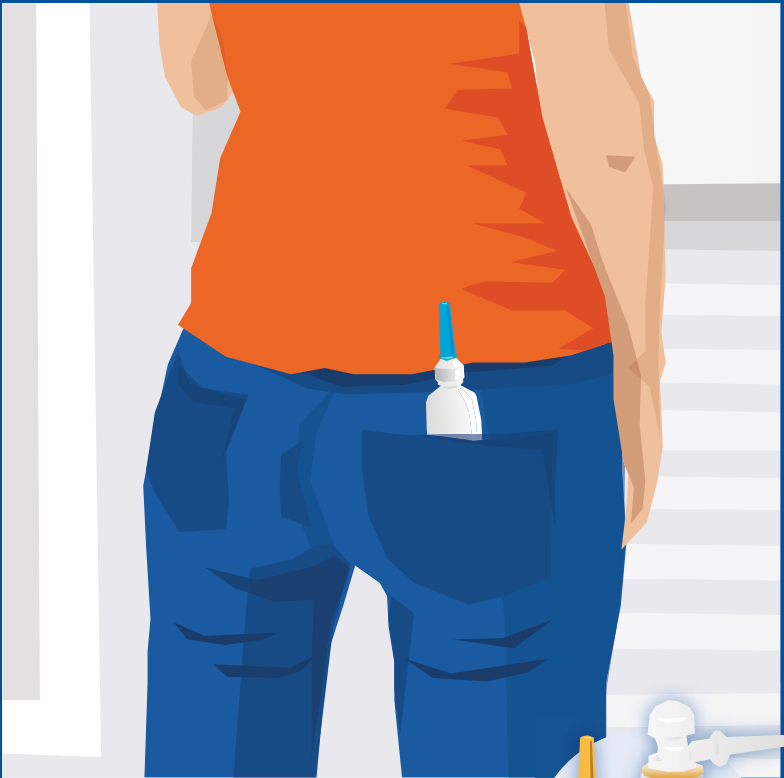


Rectal treatment for inflammatory bowel disease



Authors' addresses

Pascal Frei

Bethanien Group Practice for Gastroenterology,
Zurich, Switzerland

Gerhard Rogler

Department of Gastroenterology and Hepatology,
University Hospital, Zurich, Switzerland

Address for correspondence:

Gerhard Rogler

Klinik für Gastroenterologie und Hepatologie

UniversitätsSpital Zürich

Rämistr. 100

8091 Zürich

Switzerland

gerhard.rogler@usz.ch

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Pascal Frei
Gerhard Rogler





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Dear patient,

You have been diagnosed with an inflammatory bowel disease known as ulcerative colitis. Ulcerative colitis affects the large intestine (colon) only. The colon starts at the appendix in the lower right-hand side of the abdomen, continues upwards on the right side, turns a corner below the liver and crosses the abdomen, turns again on the left side below the spleen and then proceeds down to the rectum (see Fig. 1). It forms an upside down U in the abdominal cavity and looks a bit like a frame.

Ulcerative colitis

In ulcerative colitis, the surface of the intestinal wall – known as the mucous membrane or mucosa – becomes inflamed. This causes bloody diarrhea and abdominal cramps. In ulcerative colitis the inflammation is always most severe in the rectum; the inflammation starts at the anus and extends continuously for a varying distance into the colon (see Fig. 2). If the inflammation only affects the rectum, doctors refer to it as ulcerative proctitis or just proctitis (see Fig. 2a). If the inflammation reaches only the descending (left) colon, this is called left-sided ulcerative colitis (see Fig. 2b). If the whole colon is affected, including the ascending (right) side as far as the appendix, this is called ulcerative pan-colitis (“pan-” means “all”, Fig. 1).

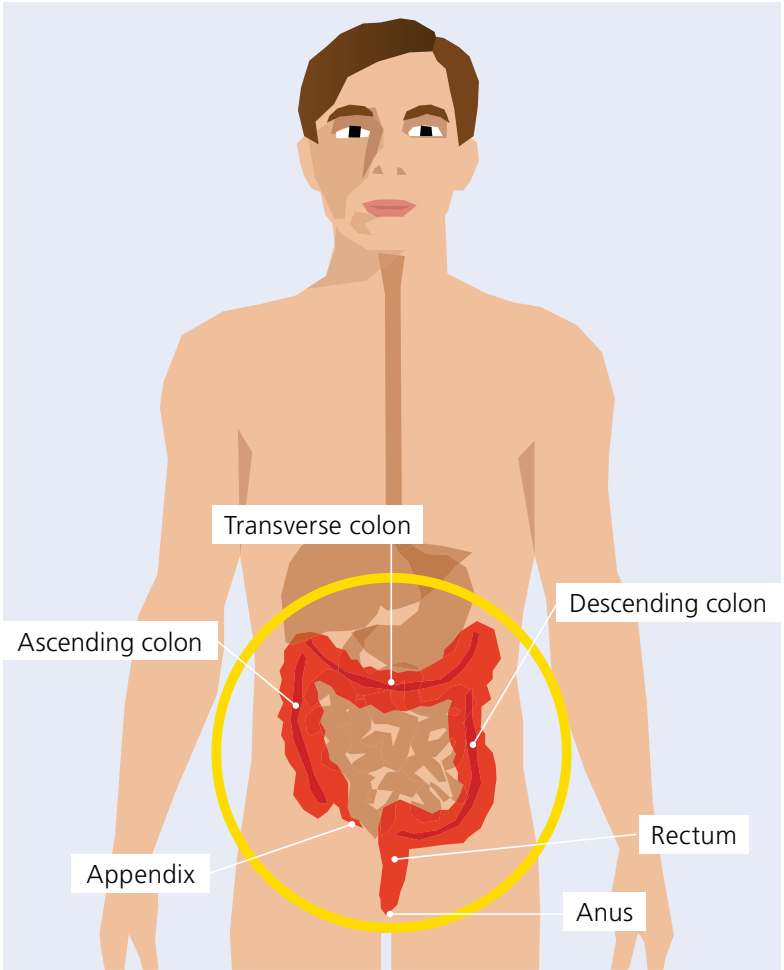


Fig. 1: Pancolitis involves inflammation of the whole colon

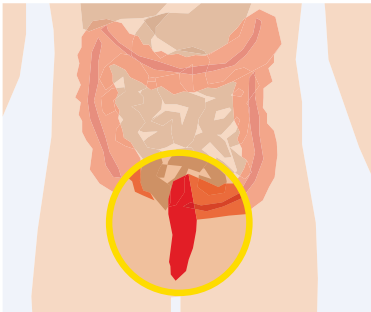


Fig. 2a: Ulcerative proctitis

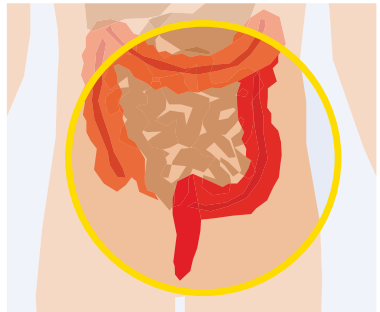


Fig. 2b: Left-sided ulcerative colitis

The basic treatment for ulcerative colitis: mesalazine

5-ASA (5-aminosalicylic acid), otherwise known as mesalazine, is the basic treatment for patients with ulcerative colitis. Mesalazine is a long-established anti-inflammatory substance that is well-tolerated by the majority of colitis patients, even when used continuously. Preparations containing mesalazine are only active when in direct contact with the inflamed mucosa (in other words, they act locally). This applies regardless of whether the preparation is swallowed in the form of tablets or granules (used orally), or inserted into the anus in the form of suppositories, enemas or foam (used rectally).

Once mesalazine has been taken up into the mucosa, it exerts its anti-inflammatory effect there and is then broken down directly while still in the mucosa. Oral preparations (tablets and granules) therefore have to be made in such a way that the mesalazine is not released until the drug reaches the colon. This depends on its galenic formulation. Preparations that are inserted into the rectum do not need to be formulated in this way. The drug is delivered directly to the site of action.

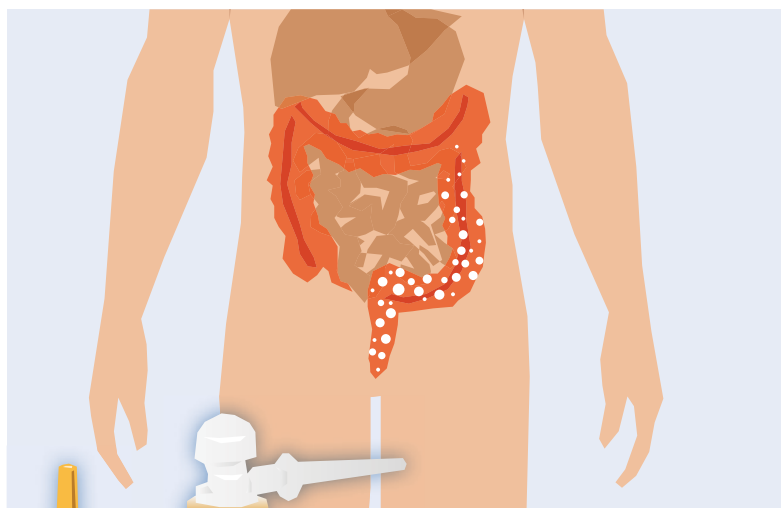
Rectal treatment, which delivers the mesalazine directly onto the inflamed mucosa, can therefore be particularly effective.

If rectal mesalazine treatment is not sufficiently effective, it is possible to use rectal cortisone/corticosteroids/steroid-containing treatments (all three names mean the same in this case). Locally-acting cortisone preparations are much better-tolerated than cortisone preparations that affect the entire body. The locally-acting cortisone preparations include those with budesonide or hydrocortisone as the active agent.

Tablet or enema?

Most colitis patients are given oral mesalazine preparations. Clinical studies of patients have shown that rectal mesalazine preparations in the form of suppositories, foam or enemas are more effective than oral mesalazine preparations, particularly in ulcerative proctitis and left-sided ulcerative colitis. This applies both to the treatment of active colitis (a flare) and to treatment to prevent another flare. In this situation the terms often used are “inducing remission” (becoming healthy and symptom-free) and “maintaining remission”, “relapse prophylaxis” or “flare prevention” (staying healthy and symptom-free). **Many studies with large groups of patients have shown that rectal treatment is prescribed and used too rarely.**

Sites of action for rectal mesalazine and rectal locally-acting cortisone preparations in the colon



Rectal preparations are given in the form of suppositories, enemas or foam and act locally on the intestinal mucosa.

This booklet aims to inform patients about the importance and usefulness of rectal treatment for ulcerative colitis, giving practical tips and clearing up misunderstandings. Only in severe forms of colitis is rectal treatment not helpful; this is because its effectiveness is reduced by frequent defecation and the strong urge to defecate, and also because it can cause pain and abdominal cramps. Whether rectal treatment is worthwhile for Crohn's disease is not clear.



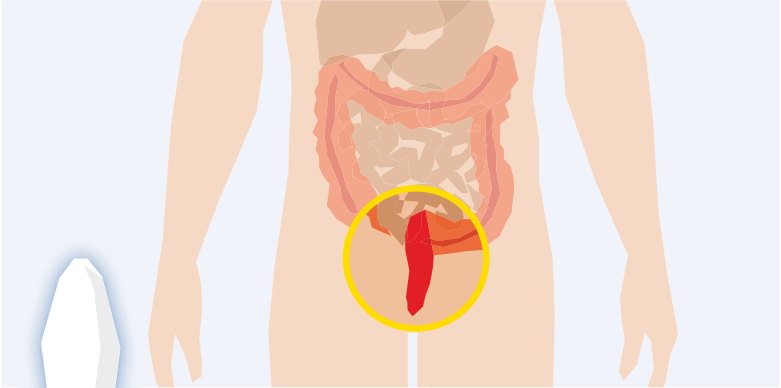
Treatment of ulcerative proctitis

Ulcerative proctitis – an inflammation that is limited to the rectum – should always be treated in the first line with mesalazine suppositories. When suppositories are used, the active ingredient coats the rectal mucosa better than when enema or foam preparations are used. Moreover, suppositories are generally better tolerated by the patient and are easier to administer.

However, all three rectal mesalazine preparations (suppositories, foams and enemas) are about equally effective in proctitis. The easiest treatment to use for proctitis is a suppository containing 1 g mesalazine once daily. Over two thirds of patients become symptom-free within 5–7 days on this treatment. A dose of more than 1 g daily in the form of suppositories probably has no additional effect and therefore does not seem worthwhile.

One 1 g mesalazine suppository daily is comparable in its effectiveness to three 500 mg suppositories daily.

In the case of ulcerative proctitis, rectal mesalazine preparations are more effective than rectal cortisone treatment. For patients with ulcerative proctitis who do not tolerate rectal mesalazine treatment, or who do not respond sufficiently, the second-line treatment is rectal administration of locally-acting cortisone preparations such as those containing budesonide or hydrocortisone. However, true intolerance to rectal mesalazine preparations is very rare.



For proctitis, suppositories are an ideal way of delivering the mesalazine to the target site.

If symptoms persist in spite of sufficient rectal treatment with suppositories, foams or enemas, a rectal cortisone preparation can also be combined with a rectal mesalazine preparation (usually with the cortisone preparation in the morning and the mesalazine preparation in the evening).

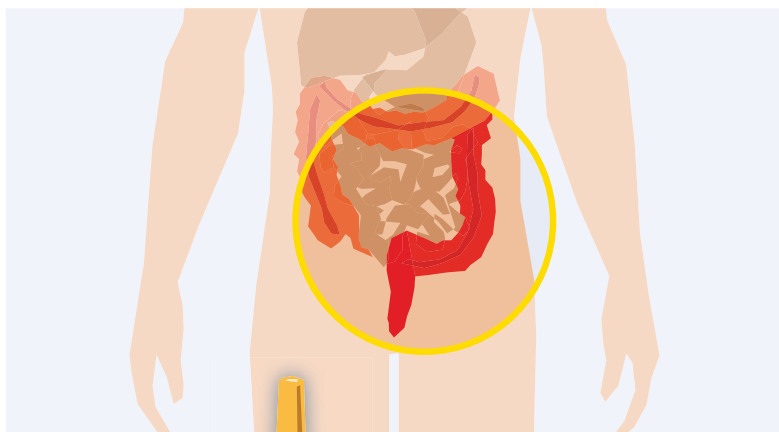
Treatment of left-sided ulcerative colitis

Like ulcerative proctitis, left-sided ulcerative colitis should first be treated rectally. Foam preparations and enemas are available for this purpose (suppositories do not spread out sufficiently to reach inflammation in the left colon, which is more than 15 cm away from the anus). The dose should be at least 1 g mesalazine/day. Enemas are available providing dosages of 1, 2 and 4 g mesalazine; foam preparations give a dosage of 1 g mesalazine per administration. As an alternative, it is possible to use cortisone preparations containing 2 mg budesonide, 100 mg hydrocortisone or 5 mg betamethasone (betamethasone is a form of cortisone acting throughout the body).

When choosing the dose, it is also important to consider the amount of fluid instilled into the rectum (the volume delivered).

Larger quantities (enemas with a volume of more than 50–60 ml) create a strong urge to defecate, so that enemas often need to be expelled into the toilet after a short time.

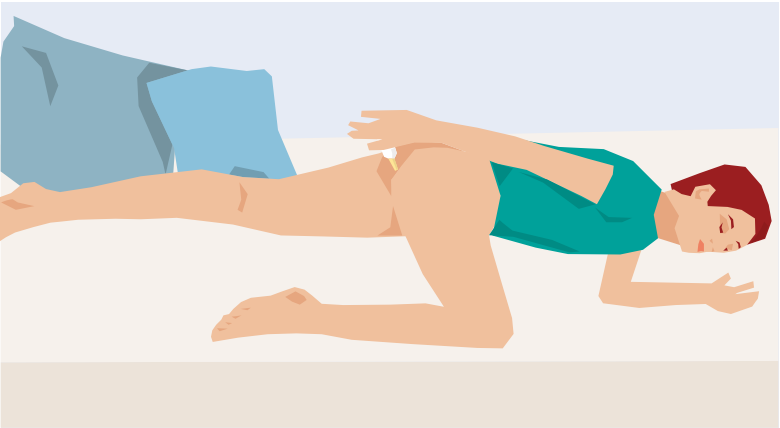
The volume delivered in rectal treatment is between 20 ml for foam preparations and up to 100 ml for enemas. The more severe the inflammation and the more damaged the mucous membrane, the greater the discomfort and urge to defecate that a higher volume can cause. For this reason, the volume of substance administered in rectal treatment should always be considered as well. Talk to your doctor about the advantages and disadvantages to find the right preparation for you.



Left-sided ulcerative colitis should be treated with enemas or foams containing mesalazine or cortisone.

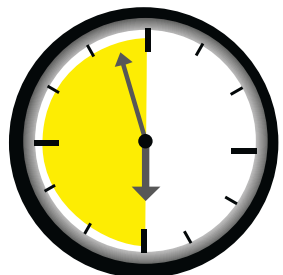
How are rectal foam or enemas used?

For treatment to be successful the method of use is important. Rectal delivery – insertion of the enema or foam – should be carried out while lying on your left side.* Immediately after rectal delivery, you should stay relaxed and continue to **lie on your left side or stomach** for 20–30 minutes. To pass the time you can read, listen to music, watch TV or catch up with your friends on social networks.



How long should a rectal treatment be kept in the bowel?

It is frequently more convenient to carry out rectal treatments in the evening. At this time of day, it is often easier to fit in the 30 minute retention period that is needed for the treatment to take effect. However, it is not necessary to keep the foam preparation or the enema in the bowel overnight. Rectal treatment does not need to fill up the intestine for several hours, but rather to coat it efficiently. You should therefore release the remaining fluid into the toilet after at least 30 minutes

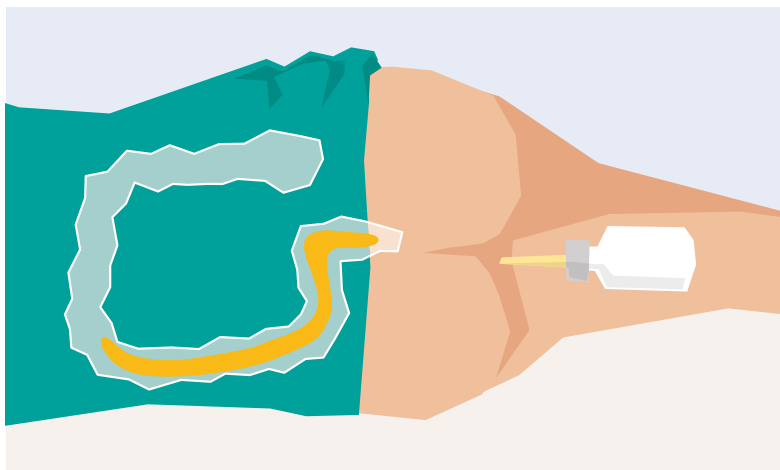


or before you go to sleep. This also has the advantage that you can sleep more peacefully because you do not need to worry about losing drug or stool in your sleep.

If you find it difficult to retain the rectal treatment for 30 minutes, talk to your doctor about supplementary medication.

It is important to remember that sitting or standing immediately after rectal administration will make the preparation collect in the rectum and cause a strong urge to defecate (because of their consistency, foam preparations may have an advantage over enemas in this respect). The preparation is then naturally unable to act because it is no longer distributed over the whole inflamed area.

If you lie on your left side or stomach, the preparation can spread upwards and achieve good cover in the left colon. Studies have shown that rectal treatment is very well distributed in the colon within 30 minutes if this procedure is followed.



When lying on the left side, the bowel mucosa is ideally coated.

* See pages 22–23 for more information about the procedure.

What if rectal treatment is not sufficiently effective?

If rectal mesalazine treatment does not bring satisfactory improvement in the symptoms of left-sided ulcerative colitis, rectal treatment should be combined with oral mesalazine, as for ulcerative proctitis. Alternatively, it may be helpful to combine rectal mesalazine with a rectal, locally-acting cortisone treatment such as a budesonide or hydrocortisone preparation. Cortisone foams and enemas are available for this purpose.

The combination of oral and rectal mesalazine treatment increases the chance of becoming symptom-free (achieving remission).

In a study by Safdi et al. (Am J Gastroenterol. 1997), the combination of oral and rectal mesalazine treatment led to clear (and quicker) improvement of symptoms in 88% of patients with mild to moderate ulcerative colitis; only 54% of patients improved after rectal administration of 4 g alone. Oral administration of 2.4 g alone was much less effective.

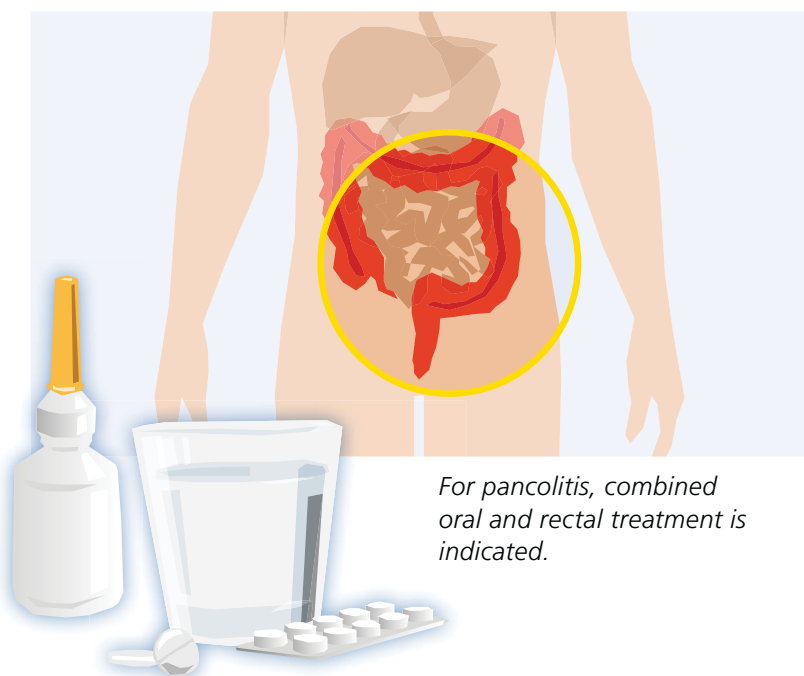
If the effect is insufficient, rectal mesalazine should be supplemented with oral mesalazine, not replaced by it.

Treatment of extensive ulcerative colitis, pancolitis

In cases of an extensive colitis involving inflammation of the transverse and ascending (right) colon, or of a pancolitis, the initial treatment strategy consists of a combination of oral and rectal mesalazine. Rectal treatment alone cannot reach the ascending colon because it is too far away from the rectum. Neither an enema nor foam is able to spread that far.

Rectal treatment is nevertheless helpful, especially for inflammation in the rectum, and acts on the main symptoms, i.e. bleeding and the urge to defecate. However, this does not apply in all cases: patients whose symptoms include severe diarrhea have poor tolerance of rectal treatment.

If pancolitis does not respond adequately to a combination of oral and rectal mesalazine, or to a combination of these with rectal, locally-acting cortisone preparations, then oral cortisone preparations should be used. However, if the patient experiences more than ten episodes of diarrhea per day, tablets and capsules will no longer be optimally dissolved. In severe cases of ulcerative colitis, rectal treatment will also have little effect. Medications that can be administered by injection are then an available option. Rectal treatment can nevertheless be started as soon as symptoms improve. The number of episodes of diarrhea drops and rectal treatment in the form of foam or an enema is tolerated for more than 20–30 minutes without a bowel movement.



For pancolitis, combined oral and rectal treatment is indicated.

Rectal treatment is also helpful for extensive ulcerative colitis or pancolitis but the decision should depend on the individual patient's symptoms.

Rectal treatment to prevent flares (“maintenance of remission”)

Rectal mesalazine is effective in preventing flares of ulcerative proctitis and left-sided colitis, and is thought to be even more effective than oral mesalazine. Most patients do not need to use rectal treatment every day to prevent flares.

One treatment every three days is often sufficient. It does not seem to matter whether rectal treatment is used on the first 7–10 days of each month, the first few days of each week, or just anytime 2–3 times per week. 1 g rectal mesalazine on each treatment day is usually sufficient to prevent flares.

A new flare always starts in the rectum. Mesalazine suppositories are therefore ideal for prevention because they release the active ingredient in exactly this area of the bowel.

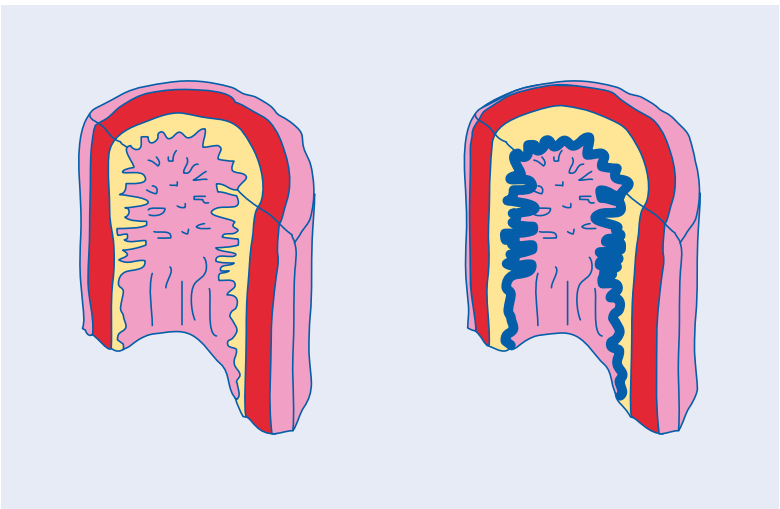
For patients who are at increased risk of repeat episodes, the combination of oral and rectal treatment seems to be better at maintaining remission than each one given as monotherapy.

Treatment with cortisone preparations does not help to keep the patient symptom-free and should be avoided.

Rectal treatment can help to heal the mucosa

Mucosal healing is a crucial objective of treatment for ulcerative colitis. Not only is it associated with fewer flares, it also reduces the risk of colon cancer (colorectal carcinoma). Rectal mesalazine treatment can lead to mucosal healing in about 50% of patients, with no difference between foam and enema preparations. Newer data also provide evidence that rectal treatment with budesonide foam preparations has the same effect.

With efficient rectal treatment you have both rapid benefit (fewer symptoms) and a long-term advantage (lower cancer risk).



Healthy mucosa

Mucosa with colitis

How long should rectal treatment be continued?

Rectal treatment should, in principle, be used for just as long as treatment with tablets or granules. Many patients adapt very well to rectal treatment. It may be irritating and perhaps a bit unpleasant at first, but it soon becomes routine. **With rectal treatment – unlike treatment with tablets – it is even possible to go for three weeks a month with no treatment at all during the flare-prevention phase.** This convinces many ulcerative colitis patients once they have made a start with rectal treatment.

The reason most often given at the start for not using rectal treatment is the urge to defecate that is caused by this form of treatment. However, this can be minimized by using low-volume preparations.

In contrast with widely-held opinion, acceptance of rectal treatment is good.

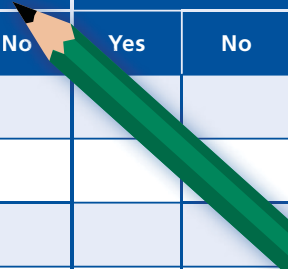


	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
Oral							
Rectal							

Patient diary

You can use the final pages of this brochure as a diary to keep a record for yourself and your doctor; you can note how the treatment works for you and record the most important information about the way your symptoms and treatment progress.

	Date	Episodes of diarrhea per day	Blood mixed in		Medication against diarrhea	
			Yes	No	Yes	No
Week 1						

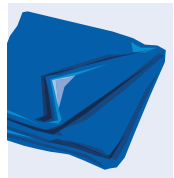


See the patient diary on page 26.

Patients often have difficulty discussing the use of rectal treatment with anyone. Please talk to your doctor. He or she is a specialist and will be glad to answer your questions. Ask a trusted friend or relative to visit the doctor with you; this can be helpful, especially at the beginning of treatment.

General tips on using suppositories, enemas and foam

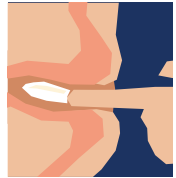
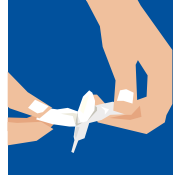
1. The best results are obtained when the bowel is emptied before the medication is used. So try to go to the toilet first if possible.
2. Use your hands to warm the bottle (with enemas) or the can (with foams) before using it. Depending on the preparation, you may also need to shake the contents vigorously. Pay attention to the information in the package insert.
3. Before starting the procedure, lay out a towel.
4. The applicator of an enema bottle or foam container is usually treated with lubricant to make it easier to insert into the anus. But you can spread additional lotion or cream on the tip if you wish.



*When using rectal preparations, the stomach muscles and pelvic floor should not be tensed. This state is easiest to achieve in a lying position. It is therefore recommended that you lie down on your left side to use enemas, foams and suppositories. Enemas and foams are best able to reach the bowel mucosa when you are in this position. **When using enemas and foams it is important to retain the preparation for 20–30 minutes while lying on your left side or your stomach.** Although the package insert for foam preparations describes administration while standing up, in practice lying down has proven to be helpful when using these preparations, too.*

Using suppositories

1. Take the suppository out of its packaging immediately before using it.
2. Lie on your side in a relaxed position.
3. Insert the suppository deep into your anus with the pointed end first.
4. If the suppository slides out, insert it again. It is important that the suppository goes a long way into the anus. You can also put on a rubber glove for the procedure.



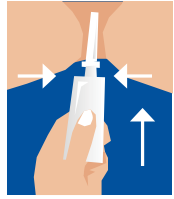
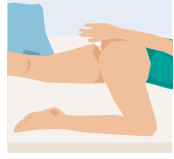
Please note: With suppositories, handling and proper storage are as vital as using the correct technique.

Handling: Always take suppositories out of their packaging with care (do not squash them). Open the packaging with scissors if necessary.

Storage: Do not store suppositories at more than 25 °C; suppositories based on fats can become soft and lose their shape at temperatures above 25 °C. A melted suppository should no longer be used.

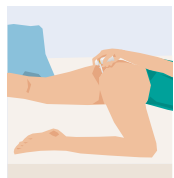
Using enemas

1. After shaking the enema for about 30 seconds, lie on your left side with your left leg stretched out and your right leg bent so that you can keep your balance.
2. Insert the applicator deep into your anus. Lean the bottle slightly downwards and then compress the bottle slowly and steadily. When the bottle is empty, slowly withdraw the applicator.
3. Immediately after this procedure stay lying down on your left side or stomach for 20–30 minutes.

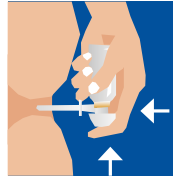


Using foams

1. Shake the spray can vigorously for about 20 seconds to mix the contents.
2. Place your index finger on the tip of the pump dome and turn the can upside down. Lie on your left side with your left leg stretched out and your right leg bent so that you can keep your balance.
3. Insert the applicator deep into your anus. Please note that the spray can is only able to function correctly when the pump dome is pointing vertically downwards.



Press the pump dome all the way in and then **release it again very slowly. The foam now enters the bowel.** It is important to remember that foam escapes when you release the pump dome!



4. Wait for 10–15 seconds before you withdraw the applicator from your anus so that all the foam can escape from the applicator. The foam expands a bit more and would otherwise escape unused from the applicator and be spilled.



5. Immediately after this procedure stay lying down on your left side or stomach for 20–30 minutes.



Please be patient if the first time is not a complete success – maybe a bit is spilled or comes straight back out of the bowel again.

! Please do not stop treatment of your own accord if the symptoms get better or disappear. Keep on with rectal treatment for as long as your doctor recommended.

Questions about using enemas



Is it normal to release some stool involuntarily?

After injecting an enema, there can sometimes be smearing of stool while fecal incontinence occurs only very rarely. It is a good idea to use the enema in the evening (see recommendations on page 15). You can go to the toilet after the 30 minute treatment period.

Do I have to continue using enemas if my symptoms get better?


It is generally recommended to continue rectal treatment until the inflammation-free state has become stable. Discuss plans for further treatment with your doctor.

Is it normal to experience pain during the procedure?

Inserting the applicator should not cause you any pain. If it feels unpleasant, you can apply additional lubricant to the applicator beforehand. You should be as relaxed as possible throughout the procedure.

Is it normal to experience bleeding during the procedure?

Insertion should not cause any bleeding. If tears (fissures) occur around the sphincter muscle it means your technique is not quite right (see page 23).



I find it hard to hold the enema liquid in my bowel for a long time before having to go to the toilet.

When you start using rectal treatment, it is normal to very quickly get the feeling that you need to go to the toilet. You should nevertheless continue with the treatment as you will still benefit even if the drug can only act for a short time. After about a week you will find it easier to hold the enema in your bowel.

Can a friend or relative give me the enema?

Some patients find it hard to use the enema themselves. If you have a friend or relative who is prepared to help you, the procedure described in this brochure should still be followed.

Patient diary

	Date	Episodes of diarrhea per day	Blood mixed in		Medication against diarrhea	
			Yes	No	Yes	No
Week 1						
Week 2						

Patient diary

	Date	Episodes of diarrhea per day	Blood mixed in		Medication against diarrhea	
			Yes	No	Yes	No
Week 3						
Week 4						



DR. FALK PHARMA GmbH



Leinenweberstr. 5
79108 Freiburg
Germany